IUCLID

Data Set

Existing Chemical	:	ID: 107-18-6
CAS No.	:	107-18-6
EINECS Name	:	allyl alcohol
EC No.	:	203-470-7
TSCA Name	:	2-Propen-1-ol
Molecular Formula	:	C3H6O

Producer related part

Company	:	Lyondell Chemical Co.
Creation date	:	01.09.2003

Substance related part

Company	:	Lyondell Chemical Co.
Creation date	:	01.09.2003
Status	:	
Memo	:	AA HPV dataset
Printing date	:	10.05.2005
Revision date	:	
Date of last update	:	10.05.2005
Number of pages	:	93
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	
Name	:	Lyondell Chemical Co.
Contact person	:	Dr Marcy I Banton
Date	:	
Street	:	One Houston Center, Suite 700, 1221 McKinney Street
Town	:	Houston, Texas TX 77010
Country	:	United States
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

26.04.2005

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name	:	
Smiles Code	:	
Molecular formula	:	C3H6O
Molecular weight	:	58.08
Petrol class	:	

07.11.2003

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	typical for marketed substance
Substance type	:	organic
Physical status	:	liquid
Purity	:	>= 99 % w/w
Colour	:	clear, colorless
Odour	:	sharp, mustard-like

25.11.2003 (30) (31)

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

propenol, 1-propen-3-ol, vinyl carbinol, 3-hydroxypropene, 2-propen-1-ol, 2-propenyl alcohol.

11.11.2003 (30)

1.3 IMPURITIES

Purity : typical for marketed substance
CAS-No :
EC-No :
EINECS-Name :
Molecular formula :
Value :

Remark : Typical impurities:
n-propanol 0.75% w/w max
water 0.30% w/w max
propionaldehyde 0.01% w/w max

03.05.2005 (30)

1.4 ADDITIVES

1.5 TOTAL QUANTITY

Remark : Allyl alcohol (CAS 107-18-6) is an intermediate chemical manufactured by Lyondell Chemical Company at sites in the U.S. and The Netherlands. Projected global production is estimated at 175 million pounds. Approximately 140 million pounds will be used captively by Lyondell for manufacture of downstream derivatives.

Allyl alcohol is also produced in Asia mainly by two Japanese producers, Showa Denka and Daicel. Estimated total Asian production is about 125 million pounds.

25.11.2003

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.6.3 PACKAGING

1.7 USE PATTERN

Remark : Allyl Alcohol is an isomer of propylene oxide, and is a bifunctional molecule used by chemical manufacturers for a multitude of purposes by reaction of the alkene

functionality, the hydroxy functionality, or both.

A significant use for Allyl Alcohol is as an intermediate in the production of 1,4-Butanediol (CAS 110-63-4) and 2-Methyl-1,3-Propanediol (CAS 2163-42-0). Other commercial uses of allyl alcohol include manufacture of allyl diglycol carbonate (CAS 142-22-3), used in optical resins; allyl glycidyl ether (CAS 106-92-3) used as silane coupling agents for a multitude of applications, such as water treatment and glass adhesion, diallyl phthalate (CAS 131-17-9), which may be used as a plasticizer, and allyl methacrylate (CAS 96-05-9) and styrene allyl alcohol (CAS 25119-62-4) resins for coatings applications.

25.11.2003

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

Remark : Occupational exposure limits:

Source/Data	ppm	mg/m^3	-- Type --	-- Notation --
US (ACGIH)/2001	0.5	1.19	8 hr TWA	Skin (Carc, N/L)
MAK (AT)/1994	2	5	8 hr TWA	Skin
	4	10	30 min STEL	Skin
OEL (BE)/2000	2	4.9	8 hr TWA	Skin
	4	9.6	15 min STEL	Skin
MAK (DA)/1996	2	5	8 hr TWA	Skin
ELV (FI)/1998	2	4.8	8 hr TWA	Skin
	4	9.6	15 min STEL	Skin
INRS (FR)/1999	2	5	8 hr TWA	Skin
	4	9.6	15 min STEL	Skin
TRGS 900/2000	2	4.8	8 hr TWA	Skin
	4	9.6	15 min STEL	Skin
ELV (IE)/1999	2	5	8 hr TWA	Skin
	4	10	15 min STEL	Skin
OEL (IT)/1999	2	4.8	8 hr TWA	Skin
	5	12.1	15 min STEL	Skin
MAC (NL)/2000	2	5	8 hr TWA	Skin
ELV (NO)/1996	2	5	8 hr TWA	Skin, Sen

VAL (ES)/2000	0.5	1.2	8 hr TWA	Skin
TLV (SE)/2000	2	5	8 hr TWA	Skin
	6	14	15 min STEL	Skin
SUVA/1999	2	5	8 hr TWA	Skin
	4	10	15 min STEL	Skin
EH40 (OES)/2000	2	4.8	8 hr TWA	Skin
	4	9.7	15 min STEL	Skin

03.05.2005 (30)

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Value : = -129 °C

Test substance : Described as allyl alcohol; no further information available.
Reliability : (2) valid with restrictions
Secondary literature (handbook or compilation of data)
03.11.2003 (18) (25) (44)

2.2 BOILING POINT

Value : = 97 °C at

Test substance : Described as allyl alcohol; no further information available.
Reliability : (2) valid with restrictions
Secondary literature (handbook or compilation of data)
03.11.2003 (45)

Value : = 96.9 °C at

Test substance : Described as allyl alcohol; no further information available.
Reliability : (2) valid with restrictions
Secondary literature (handbook or compilation of data)
03.11.2003 (44)

2.3 DENSITY

Type : density
Value : = .854 g/cm³ at °C

Test substance : Described as allyl alcohol; no further information available.
Reliability : (2) valid with restrictions
Secondary literature (handbook or compilation of data)
03.11.2003 (45) (46)

Type : density
Value : = .825 g/cm³ at °C

Test substance : Described as allyl alcohol; no further information available.
Reliability : (2) valid with restrictions
Secondary literature (handbook or compilation of data)
03.11.2003 (44)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Remark	:	Vapor Pressure = 26.1 mm Hg (experimental) Equivalent to 3,480 Pa.
Test substance	:	Described as allyl alcohol; no further information available.
Reliability	:	(2) valid with restrictions Secondary literature (handbook or compilation of data)
03.11.2003		(11)

Remark	:	23.8 mm Hg at 25 degrees C
Test substance	:	Described as allyl alcohol; no further information available.
Reliability	:	(2) valid with restrictions Secondary literature (handbook or compilation of data)
03.11.2003		(45)

Remark	:	20 mm Hg at 20 degrees C 32 mm Hg at 30 degrees C
Test substance	:	Described as allyl alcohol; no further information available.
Reliability	:	(2) valid with restrictions Secondary literature (handbook or compilation of data)
03.11.2003		(44)

Remark	:	23.5 mm Hg at 25 degrees C
Test substance	:	Described as allyl alcohol; no further information available.
Reliability	:	(2) valid with restrictions Secondary literature (handbook or compilation of data)
03.11.2003		(18)

2.5 PARTITION COEFFICIENT

Partition coefficient	:	octanol-water
Log pow	:	= .17 at °C
pH value	:	
Remark	:	Method described as 'direct'.
Test substance	:	Described as allyl alcohol; no further information available.
Reliability	:	(2) valid with restrictions Secondary literature (handbook or compilation of data)
03.11.2003		(18) (38) (44)

Partition coefficient	:	octanol-water
Log pow	:	= -.25 at °C
pH value	:	
Remark	:	CLOGP3 calculation Method: Leo and Weininger (1985) Medchem Software Release 3.33, Medicinal Chemistry Project, Pomona College, Claremont, CA.
Test substance	:	Described as allyl alcohol; no further information available.
Reliability	:	(2) valid with restrictions

Secondary literature
03.11.2003 (28)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in : Water
Value : at °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Result : Water solubility = 1E+006 g/m^3 (experimental)
Test substance : Described as allyl alcohol; no further information available.
Reliability : (2) valid with restrictions
Secondary literature (handbook or compilation of data)
03.11.2003 (11)

Solubility in : Water
Value : at °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Remark : Described as miscible;

Constant boiling mixture (BPt 87.5 degrees C) formed from 72.3% allyl alcohol + 27.7% water
Test substance : Described as allyl alcohol; no further information available.
Reliability : (2) valid with restrictions
Secondary literature (handbook or compilation of data)
03.11.2003 (46)

Solubility in : Water
Value : at °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Remark : Described as miscible.
Test substance : Described as allyl alcohol; no further information available.
Reliability : (2) valid with restrictions
Secondary literature (handbook or compilation of data)
03.11.2003 (18)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Value : = 21.1 °C
Type : open cup

Remark : Reported as 70 degrees F (open cup).
Test substance : Described as allyl alcohol; no further information available.
Reliability : (2) valid with restrictions
Secondary literature (handbook or compilation of data)
03.11.2003 (46)

Value : = 23.9 °C
Type : closed cup

Remark : Reported as 75 degrees F (closed cup).
Test substance : Described as allyl alcohol; no further information available.
Reliability : (2) valid with restrictions
Secondary literature (handbook or compilation of data)
03.11.2003 (46)

Value : = 21 °C
Type :

Test substance : Described as allyl alcohol; no further information available.
Reliability : (2) valid with restrictions
Secondary literature (handbook or compilation of data)
03.11.2003 (45)

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
Deg. product	:	
Method	:	
Year	:	1993
GLP	:	
Test substance	:	
Remark	:	Study examined atmospheric oxidation of allyl alcohol. Carbonyl products of reaction of allyl alcohol with ozone and cyclohexane, isolated as their 2,4-dinitrophenyl hydrazones, were determined using HPLC analysis (cyclohexane added to scavenge OH; reaction carried out in the dark in purified, humid air). Carbonyl products' presence confirmed using 430/360 nm absorbance ratio; quantitation involved use of external standards and construction of calibration curves.
Result	:	Carbonyl products of reaction of allyl alcohol with ozone were formaldehyde (average molar yield 0.50 ± 0.03), hydroxyacetaldehyde (average molar yield 0.30 ± 0.03), and an unidentified monofunctional carbonyl formed in low yield.
Test substance	:	Described as allyl alcohol; no further information available.
Reliability	:	(2) valid with restrictions Study available for review. Experimental study. Reasonably well reported methods and results, suitable for assessment.

05.11.2003 (14)

Type	:	air
Light source	:	other: high pressure mercury vapor lamp
Light spectrum	:	= 230 - 300 nm
Relative intensity	:	based on intensity of sunlight
Method	:	100 ppm allyl alcohol vapor irradiated with light source in glass chamber. Degradation products (CO2 and CO) measured using nondispersive IR gas chromatography and gas chromatography on a molecular sieve using an ultrasound detector, respectively.
Result	:	No photolysis occurred at wavelengths > 300 nm. At wavelengths between 230 nm and 300 nm, 39.7 % of the initial concentration of allyl alcohol was broken down into CO2 and CO after 2 hrs of illumination. The concentrations of CO2 and CO after 2 hrs of illumination were 32 ppm and 87 ppm.
Test substance	:	Described as allyl alcohol; no further information available.
Conclusion	:	No photolysis is expected to occur in troposphere.
Reliability	:	(2) valid with restrictions Study available for review. Experimental study. Reasonably well reported methods and results, suitable for assessment.

31.10.2003 (21)

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight

Deg. product	:	
Method	:	
Year	:	1993
GLP	:	no data
Test substance	:	

Remark : Study examined kinetics of gas-phase reaction of ozone with allyl alcohol investigated at atmospheric pressure, ambient temperature, and in presence of cyclohexane to scavenge hydroxyl radicals produced during reaction.

Initial allyl alcohol concentration of 1.75 - 2.0 ppm, initial ozone concentrations of 174 - 200 ppb and cyclohexane concentrations of 200 or 400 ppm. Ozone was monitored continuously by ultraviolet photometry. Reaction rate constant for allyl alcohol, corrected for the measured loss of ozone to the chamber walls, was 14.4 ± 2.0 E-18 cm3/molecule/sec.

Hydroxyl radicals reaction:
Overall OH rate constant = 2.59 E-11 cm3/molecule-sec
Removal by OH half-life = 0.31 days or 7.44 hr (1.0 E6 OH/cm3)

Removal by ozone half-life = 0.23 days or 5.52 hr (100 ppb ozone)

Test substance : Described as allyl alcohol; no further information available.

Reliability : (2) valid with restrictions
Study available for review. Experimental study. Reasonably well reported methods and results, suitable for assessment.

18.11.2003 (15)

Type	:	other
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
Deg. product	:	
Method	:	
Year	:	1991
GLP	:	no data
Test substance	:	

Remark : Photoxidation half life, water = 334 d to 37 yr

Basis: "Based upon measured rate constant for reaction with hydroxyl radical in water."

Photoxidation half life, air = 2.2-22 hr

Basis: "Scientific judgment based upon estimated rate constant with hydroxyl radical in air."

Test substance : Described as allyl alcohol; no further information available.

Reliability : (2) valid with restrictions
Secondary literature (handbook or compilation of data)

03.05.2005 (19)

Type	:	other
Light source	:	

Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
Deg. product	:	
Method	:	
Year	:	1989
GLP	:	no data
Test substance	:	
Remark	:	Release of allyl alcohol to the atmosphere is expected to result mainly in reaction with photochemically generated hydroxyl radicals with estimated half lives of 6.03-14.7 hr.
Test substance	:	Described as allyl alcohol; no further information available.
Reliability	:	(2) valid with restrictions Secondary literature (handbook or compilation of data)

31.10.2003 (18)

3.1.2 STABILITY IN WATER

Remark : Allyl alcohol lacks functional groups that are susceptible to hydrolysis.
26.04.2005

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	fugacity model level I
Media	:	
Air	:	% (Fugacity Model Level I)
Water	:	% (Fugacity Model Level I)
Soil	:	% (Fugacity Model Level I)
Biota	:	% (Fugacity Model Level II/III)
Soil	:	% (Fugacity Model Level II/III)
Method	:	other: Level 1 Mackay Fugacity Model Version 2.11, August 1999 from http://www.trentu.ca/cemc/models.html.
Year	:	
Method	:	INPUT DATA: Molecular weight = 58.08 Data temperature = 25 degrees C Log Kow = 0.17 (experimental) Water solubility = 1E+006 g/m^3 (experimental) Vapour pressure = 3,480 Pa (experimental) Melting point = -129 degrees C (experimental)
Result	:	The percentage environmental distribution calculated from the above parameters using the Mackay level 1 model was as follows: Air 3.9119%

Soil 0.1257%
Water 95.9596%
Fish 7.10E-06%
Sediment 0.0028%
Suspended Sediment 8.73E-05%
Aerosol 1.35E-07%

Reliability : (2) valid with restrictions
Study performed according to accepted principles using USEPA recommended model.

10.05.2005 (2)

Type : fugacity model level III
Media :
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: Level 1 Mackay Fugacity Model Version 2.11, August 1999 from http://www.trentu.ca/cemc/models.html.
Year :

Method : The Level III program was also used, with the default model, using the same input parameters given in the preceding record.
Remark : The distribution between compartments obtained was as follows:

Release:	To air	To water	To soil
% in air	71.5%	0.0426%	0.151%
% in soil	12.4%	0.0074%	79.6%
% in water	16.1%	99.8%	20.2%
% in sediment	0.0276%	0.171%	0.0346%

The results reflect that most allyl alcohol released to the air would remain in the air. In water, allyl alcohol is not expected to sorb to sediment. If released to the soil, allyl alcohol is likely to remain in the soil.

Reliability : (2) valid with restrictions
Study performed according to accepted principles using USEPA recommended model.

21.11.2003 (2)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic
Inoculum : other: settled sewage seed
Concentration : 2.5 µg/l related to Test substance
related to
Kinetic of testsubst. : 5 day(s) = 9 %
10 day(s) = 55 %
15 day(s) = 78 %
20 day(s) = 82 %

		%
Deg. product	:	
Method	:	
Year	:	1989
GLP	:	no data
Test substance	:	
Remark	:	Results presented as percentage theoretical BOD.
Test substance	:	Described as allyl alcohol; no further information available.
Reliability	:	(2) valid with restrictions Secondary literature (handbook or compilation of data)

21.11.2003 (18)

Type	:	aerobic
Inoculum	:	
Deg. product	:	
Method	:	
Year	:	1992
GLP	:	no data
Test substance	:	
Method	:	Sludge: 30 mg/l Substance: 100 mg/l Period 2 wk (No further details)
Result	:	86% degradation by BOD
Test substance	:	Described as allyl alcohol; no further information available.
Reliability	:	(2) valid with restrictions Secondary literature (handbook or compilation of data)

18.11.2003 (25)

Type	:	aerobic
Inoculum	:	
Deg. product	:	
Method	:	
Year	:	1995
GLP	:	no data
Test substance	:	
Method	:	ORIGIN OF SAMPLE Sediment and water was collected from Kern County Canal, an irrigation canal in an agricultural region of California, USA. Sediment was sandy loam with 0.5% organic matter. DEGRADATION TEST 1:2 sediment to water ratio in 2 Erlenmeyer flasks fitted with Dreschel caps with inlet and outlet ports for air (aerobic biodegradation test). [14C]acrolein (15 mg/L) added using a gastight syringe to the water phase of each test system. Experiment carried out in dark at 25 ± 1°C. Each flask was connected to a series of trapping vessels to collected biodegradation products: one Tenax trap to collect volatile products and two 1.0 N NaOH traps to collect [14C]CO2. ANALYTICAL METHODS Three HPLC-RAM methods were used to separate acrolein and its degradation products in the water, sediment, and the traps: ion exchange chromatography, reversed phase

chromatography, and anion-exchange chromatography. Liquid scintillation counting was used to confirm HPLC-RAM recoveries. Analytical reference standards included oxalic acid, malonic acid, glyceric acid, glyceraldehyde, glycidol, allyl alcohol, aconitic acid, lactic acid, glycerol, 3-hydroxypropanal, 1,3-propanediol, acrylic acid, and acrolein.

Remark : Allyl alcohol was a transient breakdown product of acrolein. Propanol was a transient breakdown product of allyl alcohol. Oxalic acid was a stable breakdown product of allyl alcohol and propanol. Aerobic microbial biomass at the conclusion of study was 5 x 107 cfu/g sediment.

Result : [14C]acrolein was reduced to allyl alcohol, which was further degraded to oxalic acid and CO2.

Test substance : Radiolabeled [2,3-^14C] acrolein, lot 032H9223, specific activity 16.4 mCi/mmol from Sigma. Radiochemical purity 92.2% (HPLC).

Conclusion : Under aerobic test conditions, allyl alcohol was degraded by sediment microorganisms.

Reliability : (2) valid with restrictions
Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

15.11.2003 (40)

Type : anaerobic
Inoculum :
Deg. product :
Method :
Year : 1995
GLP : no data
Test substance :

Method : ORIGIN OF SAMPLE
Sediment and water was collected from Kern County Canal, an irrigation canal in an agricultural region of California, USA. Sediment was sandy loam with 0.5% organic matter.

DEGRADATION TEST
1:2 sediment to water ratio in 2 Erlenmeyer flasks fitted with Dreschel caps with inlet and outlet ports for nitrogen (anaerobic biodegradation test) exchange. [14C]acrolein (15 mg/L) added using a gastight syringe to the water phase of each test system. Experiment carried out in dark at 25 ± 1°C. Each flask was connected to a series of trapping vessels to collected biodegradation products: one Tenax trap to collect volatile products and two 1.0 N NaOH traps to collect [14C]CO2.

Analytical methods
Three HPLC-RAM methods were used to separate acrolein and its degradation products in the water, sediment, and the traps: ion exchange chromatography, reversed phase chromatography, and anion-exchange chromatography. Liquid scintillation counting was used to confirm HPLC-RAM recoveries. Analytical reference standards included oxalic acid, malonic acid, glyceric acid, glyceraldehyde, glycidol, allyl alcohol, aconitic acid, lactic acid, glycerol, 3-hydroxypropanal, 1,3-propanediol, acrylic acid, and acrolein.

Remark : Allyl alcohol was a transient breakdown product of acrolein. Propanol was a transient breakdown product of allyl alcohol.

Oxalic acid was a stable breakdown product of allyl alcohol and propanol. Anaerobic microbial biomass at the conclusion of the study was 3 x 107 cfu/g sediment.

Result : Under anaerobic aquatic conditions, [14C]acrolein was reduced to allyl alcohol, which was further degraded to propanol and ultimately to oxalic acid and CO2.

Test substance : Radiolabeled [2,3-^14C] acrolein, lot 032H9223, specific activity 16.4 mCi/mmol from Sigma. Radiochemical purity 92.2% (HPLC).

Conclusion : Under anaerobic test conditions, allyl alcohol was degraded by sediment microorganisms.

Reliability : (2) valid with restrictions
Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

21.11.2003 (40)

3.6 BOD5, COD OR BOD5/COD RATIO

BOD5

Method : other: APHA Standard Method No 219 (1971)

Year : 1979

Concentration : related to

BOD5 : mg/l

GLP : no

COD

Method : other: ASTM D 1252-67 (1974)

Year : 1979

COD : mg/g substance

GLP : no

Method : BOD
Tests were conducted in accordance with the standard dilution method of APHA at 20 degrees C for 5 d. Allylthiourea (0.5 mg/l) was added to inhibit nitrification. Filtered effluent (10 ml; unadapted) from a waste water treatment plant was used as inoculum, in a total volume of 500 ml. Glucose and glutamic acid were run in parallel as control substances. (No further details)

COD
Tests were performed in accordance with the standard potassium dichromate method described by ASTM. (No further details)

ThOD
Theoretical oxygen demand was obtained by calculation. (No further details)

Result : ThOD = 2.21 g/g

BOD = 1.79 g/g (81% of ThOD)

COD = 2.12 (96% of ThOD)

Test substance : Described as allyl alcohol; no further information available.

Reliability : (2) valid with restrictions
Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

22.10.2003 (3)

BOD5

Method	:	other: standard dilution method
Year	:	1955
Concentration	:	related to
BOD5	:	mg/l
GLP	:	no
Remark	:	BOD (10 d) = 1.6 g/g (using sewage seed) Source reference: Mills, EJ and Stack, VT jr (1953) Biological oxidation of synthetic organic chemicals. Proceedings of the 8th Purdue Industrial Waste Conference (1953), p 492 (Unavailable for review)
Reliability	:	(2) valid with restrictions Secondary literature

22.10.2003 (20)

3.7 BIOACCUMULATION

Species	:	other: predicted value
Exposure period	:	at °C
Concentration	:	
BCF	:	= 3.16
Remark	:	METHOD BCFWin v2.14 in EPIWin v3.10 from the USEPA and Syracuse Research Corporation, as described by Meylan et al. (1999). INPUT DATA CAS No. 107-18-6 Log Kow = 0.17 (from EPIWin experimental database) RESULTS Estimated BCF = 3.162 (log BCF = 0.500)
Conclusion	:	Allyl alcohol is not likely to bioaccumulate.
Reliability	:	(2) valid with restrictions Study performed according to accepted principles using USEPA recommended model.

18.11.2003 (1) (11) (33)

3.8 ADDITIONAL REMARKS

Memo	:	Predicted half-life in air
Remark	:	Predicted air half life = 2.2-22 hr Basis: "Scientific judgment based upon estimated photooxidation half-life in air."
Reliability	:	(4) not assignable Secondary literature (handbook or compilation of data)

04.11.2003 (19)

Memo	:	Predicted half-life in surface water
Remark	:	Predicted surface water half life = 2-14 d Basis: "Scientific judgment based upon estimated

unacclimated aqueous aerobic biodegradation half-life."

Reliability : (4) not assignable
Secondary literature (handbook or compilation of data)

04.11.2003 (19)

Memo : Predicted aqueous half life (aerobic biodegradation)

Remark : Predicted aerobic half life (biodegradation) = 1-7 d

Basis: "Scientific judgment based upon estimated unacclimated aqueous aerobic biodegradation screening test data."

Removal/secondary treatment = 73%

Basis: "Based upon biological oxygen demand results from activated sludge dispersed seed aeration treatment simulator."

Reliability : (4) not assignable
Secondary literature (handbook or compilation of data)

04.11.2003 (19)

Memo : Predicted aqueous half life (anaerobic biodegradation)

Remark : Predicted anaerobic half life (biodegradation) = 4-28 d

Basis: "Scientific judgment based upon estimated unacclimated aqueous aerobic biodegradation half life."

Reliability : (4) not assignable
Secondary literature (handbook or compilation of data)

04.11.2003 (19)

Memo : Predicted half-life in soil

Remark : Predicted soil half life = 1-7 d

Basis: "Scientific judgment based upon estimated unacclimated aqueous aerobic biodegradation rate."

Reliability : (4) not assignable
Secondary literature (handbook or compilation of data)

04.11.2003 (19)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	other: Acute toxicity - fish
Species	:	Pimephales promelas (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC50	:	= .32 calculated
Limit test	:	
Analytical monitoring	:	no
Method	:	
Year	:	1986
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Method :

EXPOSURE CONDITIONS
Static multi-species bioassays were performed in seamless Pyrex glass vessels (30.5 x 30.5 x 30.5 cm) containing 20 l test solution. Water (industrial service water, Lake Ontario) was active-carbon-filtered, dechlorinated and tempered before use; total hardness 130 mg/l; pH 7.4 (detailed chemical composition provided). Determinations of the temperature, dissolved oxygen and pH of each test solution were made (but not reported) in conjunction with the daily biological observations. Test temperature target was 20 ± 1ºC. If the dissolved oxygen fell below 40% of the starting level (not reported), the test was re-run with glass sparger aeration (0.05 l/min). All tests were conducted within the extremes of 6.5 to 8.5 pH units. The photoperiod duration was 16 hours of light. The air-water interface of each tank received approximately 50 ft-c of cool-white fluorescent light.

Organisms were exposed to nominal concentrations of 0, 0.1, 1, 10 or 100 mg allyl alcohol/l test medium.

GENERAL TEST METHOD
This non-standard test method simultaneously exposed 7 organisms (pillbug, water flea, flatworm, sideswimmer, snail, segmented worm, fathead minnow) to the test substance. Fish and snails were placed free in the tanks. The remaining organism were segregated in stainless steel wirecloth basket (5.5 cm diameter x 7.5 cm depth) suspended around the circumference of the vessel (baskets raised and lowered in the water column at 1 rpm). Total biological loading (all species combined) was 0.5 g/l test medium. The water temperature during the test was 20 degrees, with a 16 hr photoperiod. Each test was performed twice.

TEST ORGANISMS
Fathead minnow (Pimephales promelas), approx. 0.2-0.5 g (10 per exposure concentration). The fish were acclimated to control diluent water in breeding/rearing tanks, and food withheld for 24 hr preceding the test.

BIOLOGICAL OBSERVATIONS
Survival, condition and behavior were recorded daily. Dead organisms were removed when observed. All species were exposed for 96 hr. If during the test more than 5/10 of any one species of test species were found dead, additional aquaria containing lower concentrations of test solution were set up.

DETERMINATION OF LC50
LC50 values were calculated (computer model) based upon the log exposure concentration and the angle transformed percent mortality.

Result : Trial 1 LC50 = 0.32 mg/l

Trial 2 LC50 = 0.32 mg/l

(Results presented in tabular form, no further information)

Test substance : Described as allyl alcohol; no further information available.

Conclusion : Under the conditions of this study (static conditions), the 96 hr LC50 for allyl alcohol in the fathead minnow (Pimephales promelas) was 0.32 mg/l.

Reliability : (2) valid with restrictions
Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

03.05.2005 (12)

Type : other: Acute toxicity - fish
Species : Carassius auratus (Fish, fresh water)
Exposure period : 24 hour(s)
Unit : mg/l
LC50 : ca. 1 calculated
Limit test :
Analytical monitoring : yes
Method : other: APHA Method 231 (1971)
Year : 1979
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : EXPOSURE CONDITIONS
Static conditions. Groups of 6 goldfish (Carassius auratus, mean length 6.2 +/- 0.7 cm, mean weight 3.3 +/- 1.0 g) were placed in all glass tanks (42 x 28 x 28 cm) containing 25 l of tap water at 20 ± 1ºC. The exposure lasted 24 hr.

Analysis of tap water was as follows (mg/l):
Cl-: 65
NO2-: 0
NO3^-: 4
SO4^2-: 35
PO4^3-: 0.15
HCO3^-: 25
SiO2: 25
NH4^+: 0
Fe: 0.05
Mn: 0
Ca^2+: 100
Mg^2+: 8
alkali: 30 (as Na^+)
pH: 7.8

ANALYSIS
The concentration of allyl alcohol in test medium was determined before and after each test, using either total organic carbon analysis or extraction/GC analysis (no further details). Comment: The concentration range used, and the recovery of added test substance, is not reported.

DETERMINATION OF LC50
Results were obtained by interpolation after plotting log exposure concentration versus mortality.

Comment: The test medium was not aerated to avoid evaporative loss of the test substance. It is noted that the oxygenation concentration did not fall below 4 mg/l.

Result : 24 hr LC50 = 1 mg/l
Test substance : Described as allyl alcohol; no further information available.
Conclusion : Under the conditions of the test, the 24 hr LC50 of allyl alcohol in goldfish is 1 mg/l.
Reliability : (2) valid with restrictions
Study available for review. Pre-guideline, non-GLP study investigation. Only limited information available but supports overall hazard assessment.

03.05.2005 (4)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : other: Acute toxicity - aquatic invertebrate
Species : Daphnia magna (Crustacea)
Exposure period : 96 hour(s)
Unit : mg/l
EC50 : = .25 - .4 calculated
Analytical monitoring : no
Method :
Year : 1986
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : EXPOSURE CONDITIONS
Static multi-species bioassays were performed in seamless Pyrex glass vessels (30.5 x 30.5 x 30.5 cm) containing 20 l test solution. Water (industrial service water, Lake Ontario) was active-carbon-filtered, dechlorinated and tempered before use; total hardness 130 mg/l; pH 7.4 (detailed chemical composition provided). If the dissolved oxygen fell below 40% of the starting level (not reported), the test was re-run with glass sparger aeration (0.05 l/min).

Organisms were exposed to nominal concentrations of 0, 0.1, 1, 10 or 100 mg allyl alcohol/l test medium.

GENERAL TEST METHOD
This non-standard test method simultaneously exposed 7 organisms (pillbug, water flea, flatworm, sideswimmer, snail, segmented worm, fathead minnow) to the test substance. Fish and snails were placed free in the tanks. The remaining organism were segregated in stainless steel wirecloth basket (5.5 cm diameter x 7.5 cm depth) suspended around the circumference of the vessel (baskets raised and lowered in the water column at 1 rpm). Total biological loading (all species combined) was 0.5 g/l test medium. The water temperature during the test was 20 ± 1ºC, with a 16 hr photoperiod. Each test was performed twice.

TEST ORGANISMS
The first and second larval instar of the water flea

(daphnia magna, 10 per exposure concentration) was used in this investigation. The organisms were acclimated to control diluent water in breeding/rearing tanks, and food withheld for 24 hr preceding the test.

PHYS-CHEM PARAMETERS
Water temperature, dissolved oxygen and pH were recorded daily (but not reported).

BIOLOGICAL OBSERVATIONS
Survival and behavior were recorded daily. Dead daphnia were removed when observed. All species were exposed for 96 hr. If during the test more than 5/10 of any one species of test species were found dead, additional aquaria containing lower concentrations of test solution were set up.

DETERMINATION OF LC50
LC50 values were calculated (computer model) based upon the log exposure concentration and the angle transformed percent mortality.

Result : Trial 1 LC50 = 0.25 mg/l

Trial 2 LC50 = 0.40 mg/l

(Results presented in tabular form, no further information)

Test substance : Described as allyl alcohol; no further information available.

Conclusion : Under the conditions of this study (static conditions), the 96 hr EC50 for allyl alcohol in the water flea (Daphnia magna) was in the range 0.25-0.40 mg/l.

Reliability : (2) valid with restrictions
Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

03.05.2005 (12)

Type : other: Acute toxicity - aquatic invertebrate
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
EC50 : = 1.65 measured/nominal
EC50 (24 hr) : = 3.66 measured/nominal
Analytical monitoring : yes
Method : other: OECD Guideline 202 (Part I) - Daphnia sp., Acute immobilization test and reproduction test
Year : 2005
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : EXPOSURE CONDITIONS
Static bioassays were performed in 250-mL glass beakers containing 200 mL of test water. Water was aged laboratory fresh water prepared by blending naturally hard well water with well water that was demineralized by reverse osmosis.

Organisms were exposed to nominal concentrations of 0 (control), 0.33, 0.65, 1.3, 2.5, 5.0, or 10 mg allyl alcohol/L test medium. Measured mean test concentrations adjusted for analytical recovery were < 0.040 (control, sample quantitation limit), 0.373, 0.516, 1.06, 2.58, 4.85, or 10.5 mg/L. All test solutions appeared clear with no color associated with the test substance, and no visible precipitates, surface films, or undissolved test substance.

GENERAL TEST METHOD
Each treatment was replicated four times. The test beakers were placed in a temperature controlled water bath. Fluorescent lighting was maintained on a 16-hour daylight photoperiod with 30-minute simulated dawn and dusk periods. The light intensity, measured with a LI-COR Model LI-189 light meter equipped with a photometric sensor, ranged from 600 to 718 lux. The test was conducted for 48 hours commencing when daphnids were added to the test chambers. Daphnids were impartially added one at a time to labeled containers until each contained 5 daphnids. Each container was randomly assigned to a treatment replicate using a random number generator. Daphnids were then transferred from the containers to the appropriate test chamber, beginning with the control test chambers and proceeding to the highest test substance treatment. Five daphnids were transferred to each test chamber resulting in a total of 20 daphnids for control and test substance treatment. Impartial placement of daphnids was completed within 30 minutes after preparation of test solutions. Daphnids were observed for immobilization and sub lethal responses once every 24 hours thereafter for the remainder of the test. At approximately 24 hours after initiation, the daphnids were transferred from the old solutions (prepared at initiation) into new solutions (prepared 24 hours after initiation).

TEST ORGANISMS
First instar Daphnia magna neonates (< 24 hours old) obtained from an in-house culture < 24 hours prior to beginning of the test were used in this investigation. The organisms were not acclimated as the daphnids were cultured under test conditions. The daphnids were not fed during the test.

WATER QUALITY
Water temperature, dissolved oxygen and pH were recorded daily. Water quality parameters remained within acceptable limits for Daphnia magna throughout the test. Water temperature during the 48 hour exposure ranged from 19.7-21.0 ºC. Dissolved oxygen concentrations ranged from 8.1-9.0 mg/L during the test, representing 93-103% of saturation. The pH of the test solutions ranged from range 8.4-8.6. Hardness, alkalinity and conductivity, measured in a sample of the dilution water at test initiation and approximately 24 hours after initiation were 150 and 156 mg/L as CaCO3, 164 and 168 mg/L as CaCO3, and 315 and 316 uS, respectively.

BIOLOGICAL OBSERVATIONS
Observations of immobilization and/or mortality were recorded for all treatments. Observations were made at 24 and 48 hours from test initiation. Water fleas counted as dead were those that were immobilized (i.e., no observed movement of appendages or post abdomen within 15 seconds after gentle agitation of the test chamber or direct gentle disturbance of the daphnid).

ANALYTICAL CONFIRMATION
Samples were collected from the parent solutions prepared at 0 and 24 hours, and from pooled aged solutions at 24 and 48 hours. The pooled aged solution samples were collected after combining replicate test solutions by treatment. The fresh control and all fresh test substance treatments were sampled at 0 hour and the aged control and all test substance treatments sampled at 24 hours. The 24-hour fresh and 48-hour aged control and test substance treatments were sampled with the exception of the 10 mg total product treatment which was not sampled due to 100% immobilization in this treatment following 24 hours of exposure. Sampling began with the control and continued up to the highest test substance treatment. Each sample volume was approximately 50 mL. Each sample was acidified to ph <2.0 with HCL. Each acidified sample was

transferred into an appropriately labeled clear, glass, 40 mL vial, filling the vial completely, and sealing the vial with no headspace. Samples were shipped to Environmental Chemistry, Inc (Houston, Texas) for analyses. The samples were analyzed in accordance with EPA Method 8620 using GC/MS. Sample introduction was accomplished using the heated purge and trap Method 5030.

STATISTICAL ANALYSIS
Statistical analysis of the nominal concentrations versus immobility data was performed using an EC50 SAS program. The program calculated the EC50 statistic and its 95% confidence limits using the probit method and Spearman-Karber method. Since the probit method could not perform the EC50 calculations based on the observed immobilization during the test, the values of the untrimmed Spearman-Karber method were reported. The no-observable-effect-concentration (NOEC) was based on the absence of any abnormal (sub lethal) effects or immobility. The slope of the concentration-response line was calculated by least-squares regression analysis of immobilization versus log of the nominal concentration.

Result : After 48 hours of exposure, immobility was 0, 0, 0, 0, 100, 100, and 100% in the 0 (control), 0.33, 0.65, 1.3, 2.5, 5.0, and 10 mg/L treatments, respectively. Quiescence was observed in the 2.5 and 5.0 mg allyl alcohol/L treatments at 24 hours. No other sub lethal effects were observed during the exposure.

Results Based on Nominal Concentrations:

24-Hr EC50: 3.7 mg/L (95% confidence limits: 3.4 and 3.9 mg/L)
48-Hr EC50: 1.8 mg/L (95% confidence limit estimates: 1.3 and 2.5 mg/L)
48-Hr NOEC based on absence of immobility and sub lethal effects: 1.3 mg/L
Slope of the 48-Hr Concentration-Response Line: 16

Results Based on Mean Measured Concentrations
(Adjusted for Analytical Recovery):

24-Hr EC50: 3.66 mg/L (95% confidence limits: 3.42 and 3.92 mg/L)
48-Hr EC50: 1.65 mg/L (95% confidence limit estimates: 1.06 and 2.58 mg/L)
48-Hr NOEC based on absence of immobility and sub lethal effects: 1.06 mg/L

Test substance : Allyl alcohol; 99.38% (Lyondell lot number CX30609214)

Conclusion : Under the conditions of this study (static conditions) and based on the nominal concentrations, the 24 and 48 hour EC50 for allyl alcohol in the water flea (Daphnia magna) were 3.7 mg/L and 1.8 mg/L, respectively, while the 48 hour NOEC was 1.3 mg/L.

Under the conditions of this study (static conditions) and based on the adjusted mean measured concentrations, the 24 and 48 hour EC50 for allyl alcohol in the water flea (Daphnia magna) were 3.66 mg/L and 1.65 mg/L, respectively, while the 48 hour NOEC was 1.06 mg/L.

The slope of the concentration-response line at 48 hours was 16.

Reliability : (1) valid without restriction
Guideline, GLP study. No circumstances occurred that would have affected the quality and integrity of the data.

10.05.2005 (16)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : other algae: Pseudokirchneriella subcapitata (green algae)

Endpoint	:	growth rate
Exposure period	:	72 hour(s)
Unit	:	mg/l
EC50	:	= 5.38 measured/nominal
EC50 Biomass	:	= 2.25 measured/nominal
Limit test	:	
Analytical monitoring	:	yes
Method	:	OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year	:	2005
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method :

EXPOSURE CONDITIONS
Bioassays were performed in 250-mL Erlenmeyer flasks. The test medium was filtered (0.45 micrometers) freshwater algal growth medium prepared with laboratory reagent water and reagent grade chemicals.

The algal cells were exposed to nominal concentrations of 0 (control), 0.65, 1.3, 2.5, 5.0, or 10 mg allyl alcohol/L test medium. Geometric measured mean test concentrations adjusted for analytical recovery were < 0.040 (control, sample quantitation limit), 0.343, 0.930, 2.41, 6.03, or 9.12 mg/L. All test solutions appeared clear with no color associated with the test substance, and no visible precipitates, surface films, or undissolved test substance.

GENERAL TEST METHOD
Each treatment was replicated three times and each replicate contained 100 mL of the appropriate parent solution. An additional replicate of the lowest test substance treatment, containing 100 mL of the appropriate parent solution, was also prepared and used to evaluate incorporation of the test substance into the algal biomass. At test initiation each replicate was inoculated with 1.0 mL of an algal concentrate containing approximately 1.0 x 10E+06 cells/mL, resulting in a final density of approximately 1.0 x 10E+04 cells/mL for each flask. At 24, 48, and 72 hours, cell density was measured in all replicates of each treatment by direct microscopic counting with a hemacytometer. All cell density measurements, with the exception of the 72 hour cell density measurements, were performed ± 1 hour from test initiation. The cell density measurements at 72 hours were performed 10 minutes prior to the observation point required by the protocol, but this deviation did not affect the integrity of the study. During the three-day exposure period, the flasks were randomly positioned using a computer generated random number table and incubated at 24 ± 2ºC in a temperature controlled environmental chamber under continuous cool-white fluorescent lighting. A continuous recording of environmental chamber temperature was made from one uninoculated blank flask using an electronic datalogger with thermistor probe. Light intensity was measured daily with a LI-COR Model LI-189 light meter equipped with a photometric sensor and ranged from 8,561 to 8,679 lux. The flasks were swirled on an orbital shaker table at approximately 100 rpm throughout the test. Temperature and pH were measured in parent solutions prior to distribution of the solutions to the test flasks. At 72 hours, temperature and pH were measured in one replicate of all treatments. Temperature and pH were measured with a WTW pH 330i meter.

TEST ORGANISMS
Psudokirchneriella subcapitata (UTEX 1648) was obtained from an established laboratory culture which originated with an inoculum received from the University of Texas, Austin, Texas.

WATER QUALITY
Test solution temperature during the 72 hour exposure ranged from 22.5-

24.0 ºC. Dissolved oxygen concentrations ranged from 8.1-9.0 mg/L during the test, representing 93-103% of saturation. The pH of the test solutions at 72 hours ranged from range 7.7-9.2. The pH of the control and test substance treatments = 1.3 mg allyl alcohol/L at 72 hours devisted more than 1 pH unit from the initial pH as a result of the algal biomass present at 72 hours. The pH deviation of more than 1 pH unit did not affect the integrity of the test since acceptable growth (16X increase) was observed in the control.

BIOLOGICAL OBSERVATIONS
Cell density was determined for each replicate of the control and each test concentration at 24, 48, and 72 hours to evaluate algal growth (inhibition or enhancement). Cell density determinations were accomplished using a hemacytometer and an optical microscope. In addition to cell density determinations, microscopic examinations were conducted to determine any morphological and physical effects on the algal cells.

ANALYTICAL CONFIRMATION
Samples were collected from the control and each test substance treatment at 0 and 72 hours of the test. The 0 hour samples were collected from the parent solutions. The 72 hour samples were collected from the pooled solutions after combining replicate solutions. At 72 hours, a sample from the 0.65 mg allyl alcohol/L abiotic treatment was collected directly from the test flask. Sampling began with the control and continued up to the highest test substance treatment. Each sample volume was approximately 50 mL. Each sample was acidified to ph <2.0 with HCL. Each acidified sample was transferred into an appropriately labeled clear, glass, 40 mL vial, filling the vial completely, and sealing the vial with no headspace. Samples were shipped to Environmental Chemistry, Inc (Houston, Texas) for analyses. The samples were analyzed in accordance with EPA Method 8620 using GC/MS. Sample introduction was accomplished using the heated purge and trap Method 5030.

STATISTICAL ANALYSIS
The NOECs, based on cell density, area under the growth curve, and growth rate, were estimated using a one-way analysis of variance (ANOVA) procedure and a two-tailed Dunnett's test. The alternate hypothesis was the mean for the growth parameter was reduced or enhanced in comparison to the pooled control mean. Prior to the Dunnett's test, a Shapiro-Wilk's test and a Levene's test were conducted to test for normality and homogeneity of variance, respectively, over treatments at each time point. If the results of the Shapiro-Wilk's and Levene's test indicated normality and insignificant heterogeneity, the analysis was performed on the non-transformed raw data. In instances of non-normality or heterogeneity, a square root transformation was performed. If both the non-transformed raw data and the transformed data exhibited non-normality or inequality of variance, a non-parametric analysis of variance was performed on the ranks of the raw data values. Non-parametric analyses were performed on the 48 and 72 hour growth rate data. Parametric analyses were performed on the 24, 48 and 72 hour area under the growth curve data and the 24 hour growth rate data.

Result **:** After 72 hours of exposure, the mean cell density in the control was 118 x 10E+04 cells/mL. This value represented an increase of 118 times the initial target inoculation density and demonstrated control growth was acceptable for the test. The mean cell density at 72 hours ranged from 1.0 x 10E+04 in the 10 mg/L treatment to 124 x 10E+04 in the 0.65 mg/L treatment. Percent differences in cell density, as compared to the control, ranged from -99% in the 10 mg/L treatment to +5% in the 0.65 mg/L treatment.

Results Based on Nominal Concentrations:

Hour / EC Type / EC Value (mg/L) / 95% Confidence Limit (mg/L) / NOEC (mg/L)

24	EbC50	2.2	2.0 and 2.3	0.65
24	ErC50	2.3	2.0 and 2.7	1.3
48	EbC50	2.2	2.1 and 2.4	1.3
48	ErC50	3.3	2.7 and 3.8	1.3
72	EbC50	2.4	2.3 and 2.4	1.3
72	ErC50	3.8	3.5 and 4.0	1.3

Results Based on the Geometric Mean of the Measured Concentrations (Adjusted for Analytical Recovery):

Hour / EC Type / EC Value (mg/L) / 95% Confidence Limit (mg/L) / NOEC (mg/L)

24	EbC50	2.09	1.95 and 2.23	0.343
24	ErC50	2.26	1.90 and 2.61	0.930
48	EbC50	2.11	1.77 and 2.46	0.930
48	ErC50	5.14	4.79 and 5.50	0.930
72	EbC50	2.25	2.21 and 2.30	0.930
72	ErC50	5.38	5.28 and 5.47	0.930

Test substance : Allyl alcohol; 99.38% (Lyondell lot number CX30609214)

Conclusion : Under the conditions of this study and based on the nominal concentrations, the 72-hour EbC50 and ErC50 for allyl alcohol in green alga (Pseudokirchneriella subcapitata) were 2.4 mg/L and 3.8 mg/L, respectively, while the 78 hour NOECs were 1.3 mg/L.

Under the conditions of this study and based on the geometric mean of measured concentrations (adjusted for analytical recovery), the 72-hour EbC50 and ErC50 for allyl alcohol in green alga (Pseudokirchneriella subcapitata) were 2.25 mg/L and 5.38 mg/L, respectively, while the 78 hour NOECs were 0.930 mg/L.

Reliability : (1) valid without restriction
Guideline, GLP study. No circumstances occurred that would have affected the quality and integrity of the data.

03.05.2005 (17)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

In Vitro/in vivo	:	In vivo
Type	:	Metabolism
Species	:	rat
Number of animals		
Males	:	
Females	:	
Doses		
Males	:	
Females	:	
Vehicle	:	
Method	:	
Year	:	1972
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Method :

ANIMALS AND TREATMENTS
Male SD rats (200g) were pretreated with either saline (0.5 ml i.p.) or pyrazole (375 mg/kg bwt i.p.; inhibitor of hepatic alcohol dehydrogenase) 2 hr prior to administration of allyl alcohol (0.05 ml/kg bwt i.p.; 2.46 mCi/mmole).

Comment: Assuming a density of 0.85, this regime was equivalent to approx. 42.5 mg allyl alcohol/kg bwt.

AUTORADIOGRAPHY
Paraffin sections from liver, lung and kidney were coated with Kodak NTB-2 emulsion, developed for 4 wk and later stained with hemotoxylin and eosin. Comment: since no steps were taken to prevent extraction of unbound radiolabel from the tissue into the organic solvents used to embed the tissues, the author assumed that most of the exposed grains of the emulsion were indicative of label covalently bound to tissue sections.

COVALENT BINDING
Animals were sacrificed 6, 8 or 24 hr post-treatment with allyl alcohol. Samples of liver, lung and kidney were homogenized in 4 volumes of water, and protein/nucleic acid precipitated with an equal volume ice cold 20% trichloroacetic acid. The precipitate was extracted 5 times with 10 ml methanol (60 degrees C) to remove radioactivity (further extractions ineffective at removing any additional label). The pellet was dissolved in NaOH (1.0 N) and aliquots taken for liquid scintillation counting.

Result : Photomicrographs included in the publication show that extensive periportal necrosis was present 24 hr after administration of allyl alcohol, whereas no microscopic changes were visible in lungs or kidney (photomicrographs not presented).

Covalent binding studies demonstrated a time-dependent decrease in amount of label bound in liver, whereas little radioactivity was present in lung and kidney. Autoradiograms (included in report) demonstrated that most of the binding occurred in the periportal zone, with little present in the centrilobular region.

Inhibition of alcohol dehydrogenase fully prevented hepatic necrosis, and decreased the amount of label bound to liver by approx. 80%. Autoradiograms confirmed that binding of 14C-allyl alcohol was markedly reduced in periportal hepatocytes. Covalent binding in lung was also decreased by pretreatment with pyrazole, whereas renal binding was unaffected.

Covalent binding data:

Treatment (n)	Time (hr)	pmol 14C-allyl alcohol/mg protein		
		Liver	Lung	Kidney
Control (5)	8	119.5	16.1	10.7
Pyrazole (2)	8	21.6*	11.2	4.2
Control (2)	24	80.2	10.5	3.6
Pyrazole (2)	24	12.9*	4.9*	2.4

* P<0.05, test not stated

Test substance : Described as 14C-allyl alcohol, specific activity 2.46 mCi/mmol; no further information available.

Conclusion : Results from these studies indicate that both binding of 14C-allyl alcohol to liver macromolecules and subsequent periportal hepatic necrosis are mediated by a metabolite of allyl alcohol. This conclusion is compatible with the hypothesis that the toxic metabolite is acrolein.

Reliability : (2) valid with restrictions
Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

03.05.2005 (37)

In Vitro/in vivo : In vivo
Type : Metabolism
Species : rat
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :
Method :
Year : 1983
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : ANIMALS AND TREATMENTS
Male SD rats (200-220g; n=4) were treated (0.05 ml, i.p.) with either allyl alcohol or deuterated allyl alcohol (d2-allyl alcohol). After 24 hr, surviving animals were killed by exsanguination (blood collected in heparinised beakers) and the liver excised.

Comment: Assuming a density of 0.85, 0.05 ml is equivalent to approx. 42.5 mg/kg bwt.

ASSESSMENT OF LIVER DAMAGE
Samples of liver were fixed (buffered formalin), paraffin sections prepared and stained with hemotoxylin and eosin. Cellular damage was assessed by the method of Mitchell et al. (1973) J Pharmacol Exp Ther, 187, 185. Glutamyl-pyruvate

transferase levels (GPT) in plasma were determined by a external laboratory (Pathologists Central Laboratory, Seattle).

COVALENT BINDING
The extent of covalent binding was determined in rats given 0.05 ml (i.p.) 14C-allyl alcohol or d2-14C-allyl alcohol as described by Reid (1972): see preceding record.

IN VITRO METABOLISM
Metabolism of allyl alcohol and d2-allyl alcohol by hepatic 9000 g supernatant (+/- pyrazole; alcohol dehydrogenase inhibitor), 104,000 g cytosol (+/- disulfuram; inhibitor of aldehyde dehydrogenase) and microsomal fraction (+/- NADPH; epoxidation of allyl alcohol to glycidol) was followed using the semicarbizide reaction (formation chromophore absorbing at 257 nm). Standards containing known amounts of acrolein were run in parallel.

Result : Hepatic necrosis (score: 1.75) and plasma GPT levels (2540 mU/ml) were 7-8 fold greater at 24 hr post-treatment in rats given allyl alcohol compared to rats given an equivalent dose of d2-allyl alcohol (necrosis score: 0.25; GPT 341 mU/ml).

Covalent binding 8 hr post-treatment with 14C-allyl alcohol was 155 pmol/mg protein compared with 48 pmol/mg protein in animals given d2-14C-allyl alcohol (3 fold difference).

NADH-dependent formation of acrolein and acrylic acid was 51-96% greater when allyl alcohol was used as substrate compared to when d2-allyl alcohol was present:

	Acrolein nmol/min/mg protein			
	AA	d2-AA	AA	d2-AA
None	0.0	0.0	0.0	0.0
NADH	48.0	31.2***	46.2	30.5***
NADH/pyrazole	16.6	11.1**	14.8	10.2**

	Acrylic acid nmol/min/mg protein			
	AA	d2-AA	AA	d2-AA
None	0.0	0.0	0.0	0.0
NADH	5.0	3.1***	5.5	2.8***
NADH/pyrazole	1.8	0.0***	1.7	0.0***

** P<0.01; *** P<0.001 (test not stated)

There was no difference in the rate of appearance or disappearance of glycidol during microsomal incubation with allyl alcohol or d2-allyl alcohol.

Test substance : Deuterated (d2) allyl alcohol was prepared by custom synthesis and purified by preparative gas chromatography (>99.5% pure).

14C-allyl alcohol was purchased from ICN Chemical and Radioisotope Division (Irvine, CA) with a specific activity of 10.8 mCi/mmol.

Deuterated 14C-allyl alcohol (0.75 mCi/mmol) was prepared by micro custom synthesis from 1-14C-acrylic acid.

Conclusion : Rats given a single i.p. treatment of allyl alcohol exhibited greater hepatic necrosis, elevated levels of

plasma GPT and greater covalent binding to liver protein than rats given an equivalent dose of deuterated allyl alcohol. These differences correlated with significantly greater formation of acrolein and acrylic acid by liver fractions in vitro when allyl alcohol was substrate compared to that seen with deuterated allyl alcohol. These NADH-dependent reactions were sensitive to inhibition by pyrazole and disulfuram, indicating a role for alcohol- and aldehyde dehydrogenases in the hepatic metabolism of allyl alcohol.

Reliability : (2) valid with restrictions
Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

03.05.2005 (35)

5.1.1 ACUTE ORAL TOXICITY

Type : LD50
Value : = 70 mg/kg bw
Species : rat
Strain : Osborne-Mendel
Sex : male/female
Number of animals : 10
Vehicle : water
Doses :
Method :
Year : 1964
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Groups of young Osborne-Mendel rats (5 per sex per dose level) were fasted (18 hr) prior to administration of 2% aqueous allyl alcohol by gavage (dose levels tested not stated). Animals were observed for clinical signs and time of death only for up to 2 weeks. No information presented on body weights or necropsy findings. The LD50 was calculated according to the method of Litchfield and Wilcoxon (1949) J Pharmacol 96, 99.

Result : LD50 = 70 mg/kg bw (95% CI=63-79).

Clinical signs: depression, colorless secretion from eyes, diarrhea, unkempt appearance.

Onset of death: between 4 hr and 4 d.

Test substance : Described as allyl alcohol; no further information available.

Conclusion : Under the conditions of the test, an oral LD50 of 70 mg/kg bw was obtained in male rats given allyl alcohol by oral gavage.

Reliability : (2) valid with restrictions
Study available for review. Early investigation, briefly reported methods and findings but considered suitable for assessment.

03.05.2005 (24)

Type : LD50
Value : = 99 - 105 mg/kg bw
Species : rat
Strain : Long-Evans
Sex : male

Number of animals	:	5
Vehicle	:	water
Doses	:	75-130 mg/kg bw; 79-140 mg/kg bw
Method	:	
Year	:	1958
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Method : Graded amounts of a 1% solution of allyl alcohol were administered by gavage (dosing needle) to groups of 5 male rats (body weights: 111-143 g or 170-252 g; two studies). Surviving animals were observed for up to 10 days. No information presented on body weights. Animals that died on study and representative survivors at the end of the observation period were euthanized and subjected to necropsy. Thorough examination of tissues was made, and specimens of all viscera were preserved in 10% formalin for microscopic examination.

No further experimental details provided.

The LD50 was calculated according to the method of Weil (1952) Biometrics, 8, 343.

Result : The main clinical sign was described as apathy, along with anxiety. Coma and diarrhea preceded death in moribund animals.
Gross post mortem findings in decedent animals included:
- edema and congestion of the lungs
- visceral congestion
- presence of mucus in the intestinal tract
- discolored liver (some necrosis)
- swollen, discolored kidneys

Histopathological examination of tissue from decedent animals revealed:
- lung congestion
- liver damage (congestion and necrosis of periportal sinusoids, central pallor and necrosis)
- presence of heme casts and cloudy swelling in the kidney.

Similar (but less frequent) lesions were present in animals that survived the 10 d observation period.

Calculated oral LD50 values of 99 mg/kg bw (for animals weighing 170-252 g) and 105 mg/kg bw (for animals weighting 111-143 g) were obtained from the study.

Test substance : Supplied by Shell Chemical Company, purity 98.5%; impurities diallyl alcohol, water.

Conclusion : Under the conditions of the test, an oral LD50 of 99-105 mg/kg bw was obtained in male rats given allyl alcohol by oral gavage.

Reliability : (2) valid with restrictions
Study available for review. Early investigation, briefly reported methods and findings but considered suitable for assessment.

26.04.2005 (10)

Type	:	LD50
Value	:	= 64 mg/kg bw
Species	:	rat
Strain	:	Sherman
Sex	:	no data
Number of animals	:	
Vehicle	:	

Doses	:	
Method	:	
Year	:	1948
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	No information on methods or findings available.
Test substance	:	Described as allyl alcohol; no further information available.
Reliability	:	(4) not assignable Study available for review. Pre-guideline, non-GLP study investigation. Only limited information available but supports overall hazard assessment.

06.10.2003 (42)

Type	:	LD50
Value	:	= 96 mg/kg bw
Species	:	mouse
Strain	:	Swiss Webster
Sex	:	male
Number of animals	:	6
Vehicle	:	water
Doses	:	84-110 mg/kg bw
Method	:	
Year	:	1958
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Graded amounts of a 1% solution of allyl alcohol were administered by gavage (dosing needle) to groups of 6 male mice (17.5-22.5 g). Surviving animals were observed for up to 10 days. No further experimental details provided. The LD50 was calculated according to the method of Weil (1952) Biometrics, 8, 343.
Result	:	The main clinical sign was described as apathy preceded by excitability. Ataxia was occasionally present. Gross post mortem findings in decedent animals included: - occasional edema and congestion of the lungs - no other abnormalities present No microscopic changes were detected. The calculated oral LD50 was 96 mg/kg bw.
Test substance	:	Supplied by Shell Chemical Company, purity 98.5%; impurities diallyl alcohol, water.
Conclusion	:	Under the conditions of the test, an oral LD50 of 96 mg/kg bw was obtained in male mice given allyl alcohol by oral gavage.
Reliability	:	(2) valid with restrictions Study available for review. Early investigation, briefly reported methods and findings but considered suitable for assessment.

25.09.2003 (10)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Value	:	= 125 - 140 ppm
Species	:	rat
Strain	:	Long-Evans
Sex	:	male
Number of animals	:	6
Vehicle	:	
Doses	:	127-225 ppm (nominal)
Exposure time	:	4 hour(s)
Method	:	
Year	:	1958
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Method :

Groups of 6 male rats (100-200 g) were exposed for 1, 4 or 8 hr to 40-2300 ppm+ allyl alcohol vapor in a glass chamber (nominal volume 19.5 l). Animals were observed for 10 days post-treatment.
[+ equivalent to 95-5450 mg/m^3; based upon 1 ppm = 2.37 mg/m3; Bevan (2001), Patty's Toxicology, 5th edition, p463]

The test atmosphere was generated by passing liquid allyl alcohol via a syringe pump into an evaporation chamber through which air flowed at 8.6 to 12.9 l/min, depending on the desired exposure concentration. The atmosphere within the chamber was allowed to equilibrate to 95-99% of the desired concentration before introduction of the animals. The nominal concentration in the chamber was calculated according to Jacobs (1949) The Analytical Chemistry of Industrial Poisons, Hazards and Solvents, 2nd edition, Interscience Publishers Inc., NY.

Glass bottles of 1 l capacity containing distilled water were connected to the sampling port of the chamber and vapor drawn through the water by suction. 0.01N bromine in acetic acid and a mercuric acetate catalyst were added to the sample, the excess bromine reduced to by iodide and the iodide titrated with 0.01N thiosulfate (Reid and Beddard (1954) Analyst, 79, 456)

The LC50 was calculated according to the method of Weil (1952) Biometrics, 8, 343.

Result :

Coma and diarrhea preceded death in moribund animals.

Gross post mortem findings in decedent animals included:
- edema and congestion of the lungs
- visceral congestion
- presence of mucus in the intestinal tract
- discolored liver (some necrosis)
- swollen, discolored kidneys

Histopathological examination of tissue from decedent animals revealed:
- lung congestion
- liver damage (congestion and necrosis of periportal sinusoids, central pallor and necrosis)
- presence of heme casts and cloudy swelling in the kidney.

Similar (but less frequent) lesions were present in animals that survived the 10 d observation period.

A calculated 4 hr LC50 value of 165 ppm (nominal) was obtained from the study.

Chemical analysis of vapor drawn from the exposure chamber revealed a 15-25% loss of allyl alcohol. After correction therefore, the LC50 was in a range 125-140 ppm.

Test substance : Supplied by Shell Chemical Company, purity 98.5%; impurities diallyl alcohol, water.

Conclusion : Under the conditions of the test, an acute LC50 of 125-140 ppm (295-330 mg/m^3) was obtained for male rats exposed to allyl alcohol vapor by inhalation for 4 hr.

Reliability : (2) valid with restrictions
Study available for review. Early investigation, briefly reported methods and findings but considered suitable for assessment.

22.10.2003 (10)

Type : LC50
Value : ca. 250 ppm
Species : rat
Strain : Sherman
Sex : male/female
Number of animals : 6
Vehicle :
Doses :
Exposure time : 4 hour(s)
Method :
Year : 1949
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Six male or female Sherman rats (approx. 100 - 150 g) were exposed to allyl alcohol vapor (nominal concentrations up to 250 ppm) for 4 hr, and the animals observed for a 14 d.

The test atmosphere was generated by passing liquid allyl alcohol into an heated evaporation chamber through which metered air was forced. Rats were exposed in a 9 l desiccator fitted with inlet and outlet ports.

The reported values are nominal (based on weight of material evaporated) and not verified analytically.

Result : Tabulated summary information included in the report notes that exposure to 250 ppm allyl alcohol resulted in mortality in 2/6, 3/6 or 4/6 rats.

Test substance : Described as allyl alcohol; no further information available.

Conclusion : Under the conditions of the test, an acute LC50 of 250 ppm (590 mg/m^3) was obtained for male rats exposed to allyl alcohol vapor by inhalation for 4 hr.

Reliability : (4) not assignable
Study available for review. Pre-guideline, non-GLP study investigation. Only limited information available but supports overall hazard assessment.

15.11.2003 (8)

Type : LC0
Value :
Species :
Strain :
Sex :
Number of animals :
Vehicle :
Doses :

Exposure time	:	
Method	:	
Year	:	1932
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Three groups of white rats (sex, strain not specified) were exposed to 50 ppm (n=5), 200 ppm (n=4) or 1000 ppm (n=6) allyl alcohol vapor for 7 hr/d until death. All animals from the 1000 ppm exposure group died within 3 hr of the start of the first exposure, with signs of discomfort and labored breathing with discharge from the nose and mouth. Gross necropsy revealed hemorrhage of the lungs and, to a lesser extent, the intestinal tract, kidneys and bladder. An unspecified number of animals died following a single exposure to 200 ppm allyl alcohol, with similar clinical symptoms to those described above. At 50 ppm, all animals survived a 7 hr exposure.
Test substance	:	Described as allyl alcohol; no further information available.
Conclusion	:	Under the conditions of the test, rats survived a 7 hr exposure to 50 ppm (approx. 120 mg/m^3) allyl alcohol vapor.
Reliability	:	(4) not assignable Study available for review. Early investigation, briefly reported methods and findings, supports hazard characterization.

15.11.2003 (32)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Value	:	= 89 mg/kg bw
Species	:	rabbit
Strain	:	other: albino (no further details)
Sex	:	male
Number of animals	:	3
Vehicle	:	
Doses	:	25-200 mg/kg bw (4 treatment levels)
Method	:	
Year	:	1958
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	4 groups of 3 male rabbits (1.3-3.9 kg) were exposed to 40-250 mg/kg bw allyl alcohol. Patches of rubber dam (3x3 cm) were placed over gauze (1 cm diameter) and sealed to clipped skin using rubber cement. Allyl alcohol (25-200 mg/kg bw) was injected through the dam, onto the skin surface, and the puncture site sealed (rubber cement). The body was then further wrapped with toweling and adhesive tape to protect the dressing. Animals were observed for 10 days post-treatment. The LD50 was calculated according to the method of Weil

(1952) Biometrics, 8, 343.

Result : The main clinical sign was described as apathy, along with flushing of the skin. Ataxia and diarrhea preceded death in moribund animals.

Gross post mortem findings in decedent animals included:
- edema and congestion of the lungs
- visceral congestion
- presence of mucus in the intestinal tract
- discolored liver (some necrosis)
- swollen kidneys.

Histopathological examination of tissues from decedent animals revealed:
- lung congestion
- liver damage (congestion and necrosis of periportal sinusoids, central pallor and necrosis)
- heme casts and cloudy swelling in the kidney

Similar (but less frequent) histopathological lesions were present in animals that survived the 10 d observation period.

The calculated dermal LD50 was 89 mg/kg bw.

Test substance : Supplied by Shell Chemical Company, purity 98.5%; impurities diallyl alcohol, water.

Conclusion : Under the conditions of the test, a dermal LD50 of 89 mg/kg bw was obtained in the rabbit following 24 hr occluded exposure to allyl alcohol.

Reliability : (2) valid with restrictions
Study available for review. Early investigation, briefly reported methods and findings but considered suitable for assessment.

22.10.2003 (10)

Type : LD50
Value : = .053 ml/kg bw
Species : rabbit
Strain : no data
Sex : no data
Number of animals :
Vehicle :
Doses :
Method :
Year : 1948
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Remark : No information on methods or findings available.

Based on a density of 0.85 g/ml, this is equivalent to approx. 45 mg/kg bw.

Test substance : Described as allyl alcohol; no further information available.

Reliability : (4) not assignable
Study available for review. Pre-guideline, non-GLP study. Limitations in design and reporting but supports overall hazard assessment.

22.10.2003 (42)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	Occlusive
Exposure time	:	24 hour(s)
Number of animals	:	3
Vehicle	:	
PDII	:	
Result	:	slightly irritating
Classification	:	
Method	:	Draize Test
Year	:	1958
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Allyl alcohol (0.5 ml) was applied to intact and abraded skin (ventral surface) of 3 male albino rabbits. (It is not stated if fur at the treatment site was clipped first.) The application site was covered with gauze under a rubber dam, fastened with adhesive tape. The test site was examined 24 hr post-application.
Result	:	Slight erythema was present at the application site (intact skin) of one animal when the patch was removed (24 hr timepoint) but this had fully resolved by 48 hr. No other reactions were noted.
Test substance	:	Supplied by Shell Chemical Company, purity 98.5%; impurities diallyl alcohol, water.
Conclusion	:	Under the conditions of this test, allyl alcohol was slightly irritating to rabbit skin.
Reliability	:	(2) valid with restrictions Study available for review. Early investigation, briefly reported methods and findings but considered suitable for assessment.

17.10.2003 (10)

5.2.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Dose	:	.1 ml
Exposure time	:	4 hour(s)
Comment	:	
Number of animals	:	6
Vehicle	:	none
Result	:	irritating
Classification	:	
Method	:	Directive 84/449/EEC, B.5 "Acute toxicity (eye irritation)"
Year	:	1989
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Allyl alcohol (0.1 ml) was instilled in the eye (between lower eyelid and eyeball) of 3 adult Rsk:NZW rabbits, and

the lids held together for approx. 1 s. The other eye served as a control. Eyes were examined and responses noted at 4, 24, 48, 72, 96 and 168 hr post-instillation. Erythema, chemosis, iritis and corneal opacity were recorded according to the method of Draize et al. (1944; J Pharmac exp Ther 82, 337) under a Philips TLE 22W/29 lamp.

In a second study conducted 6 mo later (3 additional rabbits), corneal swelling (corneal thickness) was also assessed using an ultrasonic pachometer (Ophthasonic pachometer, TEKNAR Inc, St Louis, MO) and the results expressed as the mean percentage increase for all 3 animals at 24, 48 and 72 hr.

The mean scores for erythema, chemosis and corneal opacity were calculated for all 6 rabbits at 24, 48 and 72 hr.

Result : Mean results at 24, 48 and 72 hr (n):

Erythema: 2.89 (6)
Chemosis: 1.23 (6)
Corneal opacity: 2.09 (6)
Corneal swelling (thickness): 76% (3)

(Individual, animal- or time specific results not reported).

Test substance : Allyl alcohol, >99% pure, UCB, Brussels, Belgium.
Conclusion : Under the conditions of the test, allyl alcohol was irritating to rabbit eye.
Reliability : (2) valid with restrictions
Study available for review. Guideline study. Briefly reported methods and findings but considered suitable for assessment.

15.11.2003 (22)

Species : rabbit
Concentration : undiluted
Dose : .05 ml
Exposure time : 48 hour(s)
Comment :
Number of animals : 3
Vehicle :
Result : irritating
Classification :
Method : Draize Test
Year : 1958
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : Allyl alcohol (0.05 ml) was instilled into the left eye of 3 male albino rabbits.

The eyes were examined after 1 hr for signs of irritation (first unstained, then after application of 5% fluorescein sodium). Further examinations were carried our at 24 hr and 48 hr and during the subsequent week.

Result : Conjunctival erythema (affecting 3/3 rabbits) and edema (affecting 1/3 rabbits) was present 1 hr post-instillation (no numerical scores reported).

At 24 hr, conjunctival erythema (score 4-6; affecting 3/3 rabbits), corneal opacity (score 5-10; affecting 2/3) and injection of the iris (score 1; affecting 1/3) was noted.

48 hr post-instillation, conjunctival redness (score 2-6; affecting 3/3 rabbits) and corneal opacity (score 5; affecting 1/3) but no iridial effects were present.

All eyes appeared normal by the end of 1 week.

Test substance : Supplied by Shell Chemical Company, purity 98.5%; impurities diallyl alcohol, water.

Conclusion : Under the conditions of this test, allyl alcohol was irritating to rabbit eye producing reversible conjunctival redness, iridial injection and corneal opacity that persisted at least 48 hr post instillation.

Reliability : (2) valid with restrictions
Study available for review. Early investigation, briefly reported methods and findings but considered suitable for assessment.

17.10.2003 (10)

Species : rabbit
Concentration :
Dose :
Exposure time :
Comment :
Number of animals :
Vehicle :
Result : irritating
Classification :
Method :
Year : 1946
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : 0.005 ml or 0.02 ml allyl alcohol was instilled into the eye of an undefined number of rabbits.

18-24 hr later, the eye was examined in strong daylight, then re-examined after staining with fluorescein.

The following grading system was used to record any injuries present:
- corneal opacity (max. score = 6)
- keratoconus (max. score = 6)
- iris effects (max. score = 2)
- necrosis (visible after fluorescein staining; max. score = 6)
- total maximum score = 20

Result : Descriptive information presented in the report indicates that 0.02 ml allyl alcohol resulted in a total score of 5/20, while instillation of 0.005 ml resulted in a total score of 5 or less out of 20.

INTERPRETATION
The volume applied to the eye in these studies (0.005-0.02 ml) is less than that recommended in Guideline 405 (0.1 ml). A more pronounced response would be anticipated after instillation of 0.1 ml, suggesting that allyl alcohol would be irritating to the eye.

Test substance : Described as allyl alcohol; no further information available.

Conclusion : Based on the available information, allyl alcohol appears irritating to the eye of the rabbit.

Reliability : (4) not assignable
Study available for review. Pre-guideline, non-GLP study investigation. Only limited information available but

supports overall hazard assessment.

03.05.2005 (7)

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Type	:	Sub-chronic
Species	:	rat
Sex	:	male
Strain	:	Long-Evans
Route of admin.	:	inhalation
Exposure period	:	12 wk
Frequency of treatm.	:	7 hr/d, 5 d/wk
Post exposure period	:	
Doses	:	0 (air), 1, 5, 20 ppm; 0 (air), 40, 60 ppm ; 0 (air), 100, 150 ppm
Control group	:	yes, concurrent vehicle
NOAEL	:	= 20 ppm
LOAEL	:	= 40 ppm
Method	:	
Year	:	1958
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Method :

ANIMALS AND TREATMENTS
Groups of male Long-Evans rats (10/treatment level) were exposed to allyl alcohol in three separate studies using the following exposure concentrations: 0, 1, 5 or 20 ppm; 0, 40 or 60 ppm; and 0, 100 or 150 ppm. Exposures lasted 7 hr/d, 5 d/wk for a total of 60 exposures (12 wk).

The animals were exposed in stainless steel chambers (200 l capacity). Airflow within the chamber was 10.9-21.1 l/min (3-6 air changes per hour), and the temperature in the exposure room was 20-25 degrees C.

The test atmosphere was generated by passing liquid allyl alcohol via a syringe pump into an evaporation chamber through which air flowed at 8.6 to 12.9 l/min, depending on the desired exposure concentration. The atmosphere within the chamber was allowed to equilibrate to 95-99% of the desired concentration before introduction of the animals. The nominal concentration in the chamber was calculated according to Jacobs (1949) The Analytical Chemistry of Industrial Poisons, Hazards and Solvents, 2nd edition, Interscience Publishers Inc., NY.

Clinical observations: daily
Body weights: weekly
Diet: no details
Water: not specified

NECROPSY AND HISTOPATHOLOGY
At the end of the experimental period, survivors were weighed, decapitated under ether anesthesia and subject to a post-mortem examination. Livers, kidneys and lungs from all animals were weighed and preserved (10% formalin) along with samples of thyroid, heart, thymus, pancreas, spleen, adrenal

gland, testis, bladder and brain collected from alternate animals (i.e. 5/10 per treatment level). All preserved tissues were subject to microscopic evaluation.

STATISTICAL METHODS
Relative organ weights and percentage body weight gains were analyzed using Student's T-test.

Remark : Based on a conversion factor of 1 ppm = 2.37 mg/^m3 (Bevan (2001), Patty's Toxicology, 5th edition, p463), the following exposure concentrations can be derived:

ppm	mg/m^3
1	2.4
2	4.7
5	12
20	47
40	95
60	142
100	237
150	355

Result : The achieved concentration of allyl alcohol within the exposure chambers for the higher exposure conditions was:
40.7 +/- 3.2 ppm (24)
61.1 +/- 2.4 ppm (24)
103.2 +/- 8.7 ppm (22)
166.7 +/- 17.7 ppm (14)
Values given as mean +/-SD, number of determinations in parenthesis.

MORTALITY AND CLINCIAL SIGNS
Four rats from the 150 ppm group died during the first exposure, 2 were dead by the following morning and 2 died during the second exposure. The remaining 2 rats from the 150 ppm group died by the 10th exposure (end of week 2). There were 6 deaths in animals exposed to 100 ppm (time period inadequately characterized), and 1 death following 4 exposures to 60 ppm allyl alcohol.

Clinical signs in the 150 ppm group included gasping, severe depression, nasal discharge, eye irritation and corneal opacity. Similar but less intense clinical signs were present in animals exposed to 40-100 ppm. No clinical signs were present in animals exposed to 20 ppm and below.

BODY WEIGHT
Mean percentage body weight gain was statistically significantly lower in animals exposed to 20 ppm or above:
0 ppm 134%
1 ppm 133%
5 ppm 126%
20 ppm 110% (P<0.05)

0 ppm 128%
40 ppm 90% (P<0.05)
60 ppm 75% (P<0.05)

0 ppm 135%
100 ppm 75% (P<0.05)
150 ppm (no survivors at 15 wk)

RELATIVE ORGAN WEIGHTS
Relative kidney weight (g/100 g bw) was increased 8-10% in

animals exposed to 40 ppm or 60 ppm allyl alcohol vapor for 12 wk:
0 ppm 0.724
1 ppm 0.706
5 ppm 0.765
20 ppm 0.715

0 ppm 0.582
40 ppm 0.629
60 ppm 0.643 (P<0.05)

Relative lung weight (g/100 g bw) was increased after exposure to 40 ppm allyl alcohol vapor for 12 wk:
0 ppm 0.410
40 ppm 0.435 (P<0.05)
60 ppm 0.531 (P<0.05)
(No data given for lower exposures)

Relative liver weights for treated animals were indistinguishable from those of the controls.

NECROPSY, HISTOPATHOLOGY
Livers from rats exposed to 150 ppm allyl alcohol appeared hemorrhagic and the lungs pale and spotted. The kidneys appeared normal. The only microscopic observation was slight congestion of the lungs and liver (no further details).

Lesions and microscopic findings at 100, 60 and 40 ppm were described as similar but less intense to those reported at 150 ppm.

There were no unusual gross or microscopic findings at 20 ppm or below.

DERIVATION OF NOAEC
Although only limited data are available from this study, increases in relative kidney and lung weight are consistent with a LOAEC of 40 ppm. No lung data are available for animals exposed to lower concentrations, however relative kidney weights were unaffected indicating a NOAEC of 20 ppm. The NOAEC for decreased bw gain was 5 ppm.

Test substance : Supplied by Shell Chemical Company, purity 98.5%; impurities diallyl alcohol, water.

Conclusion : Under the conditions of this study, a sub-chronic inhalation NOAEC of 5 ppm (12 mg/m^3) was obtained for decreased body weight gain in rats exposed to allyl alcohol over 12 wk.
With regard to organ effects, increases in relative kidney weight were consistent with a systemic NOAEC of 20 ppm (47 mg/m^3).

Reliability : (2) valid with restrictions
Study available for review. Pre-guideline, non-GLP study. Limitations in design and reporting but supports overall hazard assessment.

15.11.2003 (10)

Type : Sub-acute
Species : rat
Sex : no data
Strain : no data
Route of admin. : inhalation
Exposure period :
Frequency of treatm. :

Post exposure period	:	
Doses	:	
Control group	:	
Method	:	
Year	:	1932
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Remark : Three groups of white rats (sex, strain not specified) were exposed to 50 ppm (n=5), 200 ppm (n=4) or 1000 ppm (n=6) allyl alcohol vapor for 7 hr/d until death.

All animals from the 1000 ppm exposure group died within 3 hr of the start of the first exposure, with signs of discomfort and labored breathing with discharge from the nose and mouth. Gross necropsy revealed hemorrhage of the lungs and, to a lesser extent, the intestinal tract, kidneys and bladder.

All animals exposed to 200 ppm allyl alcohol died following one or two exposures with similar clinical symptoms to those described above.

Rats exposed to 50 ppm allyl alcohol vapor survived an average of 30 d (no further details).

Test substance : Described as allyl alcohol; no further information available.

Reliability : (4) not assignable
Study available for review. Early investigation, briefly reported methods and findings, supports hazard characterization.

15.11.2003 (32)

Type	:	Sub-chronic
Species	:	rat
Sex	:	male/female
Strain	:	Wistar
Route of admin.	:	drinking water
Exposure period	:	15 wk
Frequency of treatm.	:	daily
Post exposure period	:	none
Doses	:	0, 50, 100, 200 or 800 ppm
Control group	:	yes, concurrent vehicle
NOAEL	:	= 50 ppm
Method	:	
Year	:	1978
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Method : ANIMALS AND TREATMENTS
Groups of Wistar rats (15/sex/treatment level) were exposed to allyl alcohol in the drinking water at 0 (control), 50, 100, 200 or 800 ppm for 15 weeks. Additional groups of 5 rats/sex were given 0, 200 or 800 ppm allyl alcohol for 2 weeks or 6 weeks.
(Comment: group sizes inconsistent with OECD TG 408)
Animal supplier: commercial supplier (not specified), SPF colony.
Housing: 5/cage; 20+/-1 degree C; 50-60% relative humidity.
Body weights: recorded pre-treatment and on days 1, 6, 8, 13, 15 or 20.
Food and water intake: measured over the 24-hour period preceding each weighing.
Diet: Spratts Laboratory Diet No 1, ad libitum

Water: not specified

RENAL FUNCTION AND URINE ANALYSIS
Renal function was investigated during wk 2 or wk 5 (n=5/sex) and in wk 15 (n=12/sex). Concentrating ability (specific gravity, volume) was determined by measuring the urine volume produced during 0-6 hr of water deprivation; at wk 5 and 15, the concentration test was extended to include samples collected over 4 hr following a 16 hr period without water. Diluting ability was then assessed over 2 hr following a water load of 25 ml/kg bwt; these samples were also assessed for specific gravity, appearance and microscopic constituents (cells) as well as a semi-quantitative evaluation of glucose, ketones, bile salts and blood. At wk 5 and 15, and studies performed after 2 wk treatment, concentrating ability was determined over 2 hr following a 6 hr deprivation period.

HEMATOLOGY
Blood collected at necropsy was assessed for hemoglobin content, packed cell volume and red cell and total leukocyte counts. A differential leukocyte count and a reticulocyte count was performed on samples from control and high dose animals. (Comment: several omissions compared with OECD TG 408.)

CLINICAL CHEMISTRY
Serum was analyzed for urea, glucose, total protein and albumin, together with ASAT, ALAT and lactic dehydrogenase activity. (Comment: several omissions compared with OECD TG 408.)

NECROPSY AND HISTOPATHOLOGY
At the end of the appropriate treatment period, animals were killed by exsanguination under barbiturate anesthesia following an overnight fast. Animals were subject to a post-mortem examination and any external or internal macroscopic abnormalities noted. The brain, pituitary, thyroid, heart, liver, spleen, kidneys, adrenals, gonads, stomach, small intestine and cecum were weighed. Samples of these organs and of salivary gland, trachea, aorta, thymus, lymph nodes, urinary bladder, colon, rectum, pancreas, uterus, skeletal muscle and any other tissue that appeared to be abnormal were fixed in 10% buffered formalin. Paraffin-wax sections of these tissues were stained with hematoxylin and eosin for histopathological investigation. (Comment: range of tissues comparable to OECD TG 408, but with some exclusions notably aorta, trachea/lungs, skin, eye, peripheral nerve, bone marrow).

STATISTICAL METHODS
Mean body weights, food and water intake and organ weights were analyzed using Student's t-test. Renal function data were analyzed by the method of White (1952; Biometrics, 8, 33).

Result **:** INTAKE OF TEST SUBSTANCE
The calculated mean intake of allyl alcohol over the course of the study (based on body weight and water intake data) was:
Males: 0, 4.8, 8.3, 14.0, 48.2 mg/kg bw/d
Females: 0, 6.2, 6.9, 17.1 and 58.4 mg/kg bw/d

BODY WEIGHT, FOOD INTAKE AND WATER CONSUMPTION
Body weight was significantly decreased in males given 100 or 200 ppm allyl alcohol from wk 2 of treatment, and from

males and females given 800 ppm following a single day's treatment. Terminal body weights (g) at week 15 were:
- Males
Control: 472
50 ppm: 453
100 ppm 449 (ns)
200 ppm: 420 (P<0.01)
800 ppm: 270 (P<0.001)
- Females
Control: 253
50 ppm: 260
100 ppm 260
200 ppm: 257
800 ppm: 205 (P<0.001)

Food intake was significantly decreased in male rats from the 200 (-11%; P<0.01) and 800 ppm (-32%; P,0.001) groups, and in high dose females (-18%; P,0.001).

There was a statistically significant decrease in water intake in all treated groups:
- Males
Control: 27.7
50 ppm: 24.2 (P<0.01)
100 ppm 19.4 (P<0.01)
200 ppm: 15.5 (P<0.001)
800 ppm: 10.0 (P<0.001)
- Females
Control: 26.5
50 ppm: 22.0 (P<0.05)
100 ppm 17.2 (P<0.001)
200 ppm: 14.4 (P<0.001)
800 ppm: 9.8 (P<0.001)

HEMATOLOGY AND CLINICAL CHEMISTRY
No abnormalities reported. (Comment: data not available for evaluation.)

RENAL FUNCTION AND URINE ANALYSIS
There was a statistically significant decrease (-50% to -75%) in excretion of cells in male rats following 2, 5 and 15 wk treatment with 800 ppm allyl alcohol.

Urine concentrating ability (ml/6 hr) was significantly impaired in a time- and dose dependent manner in males:
- Wk 2
Control: 1.9
200 ppm: 2.2
800 ppm: 0.6 (P<0.05)
- Wk 5
Control: 3.8
200 ppm: 0.9 (P<0.01)
800 ppm: 0.9 (P<0.01)
- Wk 15
Control: 4.5
50 ppm: 2.7
100 ppm: 2.4 (P<0.01)
200 ppm: 1.8 (P<0.001)
800 ppm: 0.8 (P<0.05)
Essentially similar, but statistically non-significant, changes were present in females.

Urine concentrating ability over 16-20 hr was unaffected by treatment with allyl alcohol.

Urine volume (ml) was statistically significantly decreased during the dilution test at wk 2, 5 and 15 for animals (both sexes) treated with allyl alcohol in drinking water at 200 ppm or above. Representative data for males:
- Wk 2
Control: 4.3
200 ppm: 0.7 (P<0.01)
800 ppm: 0.3 (P<0.01)
- Wk 5
Control: 7.3
200 ppm: 2.2 (P<0.05)
800 ppm: 0.9 (P<0.05)
- Wk 15
Control: 8.4
50 ppm: 7.5
100 ppm: 5.9
200 ppm: 3.6 (ns)
800 ppm: 0.5 (P<0.001)

Specific gravity was increased (approx. 1-4%) during the dilution test at wk 2, 5 and 15 for males and females given allyl alcohol in drinking water at 200 ppm or above. These changes were generally statistically significant.

POST MORTEM EXAMINATION
No gross abnormalities were present in any sex/treatment group.

Absolute organ weights were generally decreased in males, and to a lesser extent in females, in a time- and treatment related manner after ingestion of 100 ppm allyl alcohol or above. Although statistically significant (especially in high dose males), these decrements were consistent with the lower body weights recorded in treated animals. The exception was absolute kidney weight for females, which was statistically significantly increased (11-13%; P<0.001) at week 15 in the 100, 200 and 800 ppm treatment groups. Organ weight results at 15 weeks summarized below:

--abs. kidney wt--

	males	females
Control	2.42	1.48
50	2.43	1.48
100	2.48	1.65 P<0.001)
200	3.07	1.67 P<0.001)
800	2.10	1.64 P<0.001)

--abs. brain wt (g)--

	males	females
Control	1.97	1.70
50	1.95	1.75
100	1.98	1.74
200	1.89	1.74
800	1.81 (P<0.001)	1.66

--abs. heart wt (g) --

	males	females
Control	1.15	0.78

50	1.12	0.76
100	1.09	0.77
200	1.05	0.75
800	0.84 (P<0.001)	0.66 (P<0.001)

--abs. liver wt (g) --

	males	females
Control	11.02	5.87
50	11.15	5.72
100	11.29	6.21
200	9.81 (P<0.01)	5.93
800	7.93	5.63

--abs. spleen wt (g) --

	males	females
Control	0.72	0.52
50	0.75	0.55
100	0.76	0.56
200	0.71	0.54
800	0.64	0.53

--abs. stomach wt (g) --

	males	females
Control	1.64	1.26
50	1.76	1.24
100	1.79 (P<0.01)	1.34
200	1.66	1.26
800	1.44 (P<0.01)	1.33

--abs. small intestine wt (g) --

	males	females
Control	7.69	6.23
50	7.92	6.13
100	7.86	6.06
200	7.26	5.73
800	6.40 (P<0.001)	5.63

--abs. cecum wt (g) --

	males	females
Control	1.10	0.84
50	1.07	0.85
100	1.07	0.90
200	1.06	0.87
800	0.84 (P<0.001)	0.73

--abs. adrenals (mg)--

	males	females
Control	67.5	74.0
50	65.6	77.7
100	64.6	80.9
200	61.5	76.3
800	59.4	71.5

--abs. gonad wt --

	males (g)	females (mg)
Control	3.52	118.7
50	3.41	120.5
100	3.50	128.1
200	3.48	127.1
800	3.36	110.1

--abs. pituitary wt (mg) --

	males	females
Control	10.21	11.96
50	9.74	10.64
100	9.69	11.51
200	9.71	11.02
800	8.47	10.88

--abs. thyroid wt (mg) --

	males	females
Control	19.1	16.8
50	19.3	17.6
100	20.1	15.2
200	18.7	15.9
800	17.4	14.9

-- Terminal body wt (g) --

	males	females
Control	437	253
50	447	247
100	426	247
200	404 (P<0.01)	241
800	289 (P<0.001)	201 (P<0.001)

Relative organ weights (g/100 g bwt) were generally increased to a statistically significant extent in high dose animals of both sexes at study termination. Relative kidney weights and relative stomach weights, in contrast, were increased in a dose-dependent manner in females at week 2 and in both sexes following 6 or 15 weeks of treatment. Results at 15 weeks summarized below:

--rel. kidney wt (g/100g bwt) -- -

	males	females
Control	0.56	0.59
50	0.55	0.60
100	0.58	0.67 (P<0.001)
200	0.59 (P<0.01)	0.70 (P<0.001)
800	0.73 (P<0.001)	0.83 (P<0.001)

--rel. stomach wt (g/100g bwt) --

	males	females
Control	0.37	0.50
50	0.39	0.50
100	0.42 (P<0.001)	0.54 (P<0.05)
200	0.41 (P<0.01)	0.52
800	0.50 (P<0.01)	0.66 (P<0.001)

--rel. brain wt (g/100g bwt)--

	males	females
Control	0.45	0.68
50	0.44	0.71
100	0.47	0.71
200	0.47	0.72
800	0.64 (P<0.001)	0.83 (P<0.001)

--rel. heart wt (g/100g bwt) --

	males	females
Control	0.26	0.31
50	0.25	0.31
100	0.26	0.31
200	0.26	0.31
800	0.29	0.33

--rel. liver wt (g/100g bwt) --

	males	females
Control	2.52	2.33
50	2.50	2.33
100	2.65	2.51
200	2.43	2.46
800	2.74 (P<0.01)	2.75 (P<0.001)

--rel. spleen wt (g/100g bwt) --

	males	females
Control	0.17	0.20
50	0.17	0.22
100	0.18	0.23
200	0.18	0.22
800	0.22 (P<0.001)	0.25

--rel. small intestine wt (g/100g bwt) --

	males	females
Control	1.76	2.48
50	1.77	2.50
100	1.85	2.45
200	1.80	2.39
800	2.24 (P<0.001)	2.82 (P<0.01)

--rel. cecum wt (g/100g bwt) --

	males	females
Control	0.25	0.33
50	0.24	0.34
100	0.25	0.36
200	0.26	0.36
800	0.29 (P<0.05)	0.37

--rel. adrenals (mg/100g bwt)--

	males	females
Control	15.5	29.6
50	14.9	31.9
100	15.2	33.0
200	15.3	31.7
800	21.0 (P<0.001)	35.6 (P<0.01)

--rel. gonad wt --

	males (g/100g bwt)	females (mg/100g bwt)
Control	0.81	47.3
50	0.77	49.4
100	0.82	52.0
200	0.86	52.7
800	1.18 (P<0.001)	55.1

--rel. pituitary wt (mg/100g bwt) --

	males	females
Control	2.34	4.74
50	2.20	4.33
100	2.28	4.60
200	2.41	4.52
800	3.00 (P<0.01)	5.46

--rel. thyroid wt (mg/100g bwt) --

	males	females
Control	4.37	6.67
50	4.33	7.13
100	4.72	6.13

200	4.66	6.98
800	6.09 (P<0.001)	7.48 (P<0.05)

HISTOPATHOLOGICAL EVALUATION
Minor changes were present in the microscopic appearance of the liver (occasional vacuolated cells, scattered individual cell necrosis with lymphocyte infiltration), kidneys (occasional vacuolated tubular cells) and spleen (mild degree of peribronchial lymphocyte infiltration) however these occurred at a similar incidence in control and treated animals. (No microscopic changes were reported in stomach and no other details on the histopathological evaluation were noted.)

DERIVATION OF NOAEL
The majority of findings from this study, in particular lower body weights, alterations in organ weights and changes in renal function, appear secondary to a reduction in water intake that was particularly pronounced in high dose animals. This is presumed to reflect poor palatability of the dosing solutions. Against this background, there was a more generalized increase in absolute kidney weight (females), relative kidney weight (both sexes) and relative stomach weight (both sexes) in the intermediate and high dose groups after 15 weeks of treatment. While local irritation (stomach) or dehydration (kidney) may have contributed in part to these findings, they may also be indicative of mild systemic renal toxicity with a sub-chronic NOAEL of 50 ppm (6.2 mg/kg bwt/day) in females and 100 ppm (8.3 mg/kg bwt/day) in males.

Test substance : Allyl alcohol, 99% pure, SG (20 degree C) 0.849-0.852; bpt 95-98 degrees C, supplied by Bush Boake Allen Ltd, London.

Conclusion : Under the conditions of this study, a sub-chronic NOAEL of 50 ppm allyl alcohol in drinking water (equivalent to 6.2 mg/kg bw/day) was obtained for female rats and 100 ppm (equivalent to 8.3 mg/kg bwt/day) was obtained for males, based upon treatment and time related increases relative kidney weight. Possible confounding by dehydration (caused by poor palatability of the test solutions) cannot, however, be completely excluded.

Reliability : (2) valid with restrictions
Study available for review. Pre-guideline, non-GLP study. Reasonably well reported methods and results, suitable for assessment.

03.05.2005 (6)

Type : Sub-chronic
Species : rat
Sex : male/female
Strain : Long-Evans
Route of admin. : drinking water
Exposure period : 13 wk
Frequency of treatm. : continuous
Post exposure period :
Doses : 0 (water), 1, 5, 50, 100 or 250 ppm; 0, 500 or 1000 ppm
Control group : yes, concurrent vehicle
NOAEL : = 100 ppm
LOAEL : = 250 ppm
Method :
Year : 1958
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : ANIMALS AND TREATMENTS
Groups of male and female Long-Evans rats (10/sex/treatment level) were exposed to allyl alcohol in drinking water in

two separate studies using the following exposure concentrations: 0, 1, 5, 50, 100 or 250 ppm; 0, 500 or 1000 ppm. Treatment was continuous and lasted for 13 wk.

Stock solutions were prepared weekly in brown glass bottles with plastic stoppers.

Clinical observations: daily
Body weight: weekly
Water consumption: weekly
Diet: no details

NECROPSY AND HISTOPATHOLOGY
At the end of the experimental period, survivors were weighed, decapitated under ether anesthesia and subject to a post-mortem examination. Livers and kidneys from all animals were weighed and preserved (10% formalin). Samples of duodenum, thyroid, heart, thymus, pancreas, spleen, adrenal gland, testis, ovary, bladder and brain collected from alternate animals (i.e. 5/10 per treatment level). All preserved tissues were subject to microscopic evaluation.

STATISTICAL METHODS
Relative organ weights and percentage body weight gains were analyzed using Student's T-test.

Result : WATER CONSUMPTION AND INTAKE OF TEST SUBSTANCE
Water consumption decreased in a treatment-related manner in both sexes:

	--ml/rat/day--	
	males	females
0 ppm	145	177
1 ppm	131	170
5 ppm	124	188
50 ppm	118	147
100 ppm	116	133
250 ppm	102	135
0 ppm	151	172
500 ppm	82	87
1000 ppm	72	67

Calculated intake of allyl alcohol was as follows:

	--mg/kg bw/d--	
	males	females
0 ppm		
1 ppm	0.13	0.17
5 ppm	0.62	0.94
50 ppm	5.9	7.3
100 ppm	11.6	13.2
250 ppm	25.5	34.0
0 ppm		
500 ppm	41.0	43.7
1000 ppm	72.0	67.4

CLINICAL SIGNS
Occasional crusting or swelling of the eyelids was the only clinical sign observed (no detail of any dose/severity relationship).

Two males from the 250 ppm treatment group lost weight; one was sacrificed after 5 wk, the other died during week 10.

Pulmonary edema was observed in one animal at post-mortem with necrosis of the intestinal mucosa in the other; liver and kidney were normal.

NECROPSY OBSERVATIONS
Few abnormalities were noted at necropsy at week 13:
- perirenal fat was decreased in the 500 ppm group and absent at 1000 ppm
- the livers from two high dose females were pale with a soft, spongy yellowish appearance with well organized areas of necrosis with regeneration observed upon microscopic examination (appearance and distribution considered consistent with infarction by the study authors)
- perivascular cuffing present in brain from one high dose female
- the authors state there were no other findings of interest

BODY WEIGHT
Mean percentage body weight gain was statistically significantly lower in animals exposed to 500 ppm allyl alcohol in drinking water and above:

	males	females
0 ppm	76	51
1 ppm	79	56
5 ppm	98	51
50 ppm	108	60
100 ppm	92	47
250 ppm	106	42

0 ppm	229	139
500 ppm	99*	70*
1000 ppm	51*	43*

* = P<0.05

RELATIVE ORGAN WEIGHTS
Relative kidney weight (g/100 g bw) was increased in a dose related manner following 13 wk treatment with allyl alcohol in drinking water:

	males	females
0 ppm	0.817	0.776
1 ppm	0.792	0.759
5 ppm	0.816	0.766
50 ppm	0.842	0.767
100 ppm	0.829	0.794
250 ppm	0.826*	0.882*

0 ppm	0.610	0.612
500 ppm	0.760*	0.778*
1000 ppm	0.815*	0.834*

* = P<0.05

Relative liver weight (g/100 g bw) was increased 11-22% in males given allyl alcohol in drinking water at 250 ppm or above for 13 wk; less consistent increases present in females:

	males	females
0 ppm	3.02	3.59
1 ppm	2.91	3.60
5 ppm	3.01	3.62
50 ppm	3.03	3.72
100 ppm	3.32+	3.30
250 ppm	3.35*	3.46

0 ppm 3.03 3.26
500 ppm 3.50 3.66
1000 ppm 3.69* 3.41
* = P<0.05
(+ Note: value reported as 0.332; presumed type-setting error)

DERIVATION OF NOAEL
Although only limited data are available from this study, statistically significant increases in relative kidney weight in rats of both sexes given 250 ppm or above allyl alcohol in drinking water, with a concurrent decrease in body weight gain (significant at 500 ppm and 1000 ppm), appears indicative of toxicity. Relative liver weights were also increased in male rats given 250 ppm and above, although this change was no always statistically significant. These observations point to a NOAEL of 100 ppm (equivalent to 11.6-13.2 mg/kg bw/d in males and females, respectively).

Test substance : Supplied by Shell Chemical Company, purity 98.5%; impurities diallyl alcohol, water.

Conclusion : Under the conditions of this study, a sub-chronic oral NOAEL of 100 ppm allyl alcohol in drinking water (equivalent to 11.6-13.2 mg/kg bw/d) was obtained for the rat, based upon treatment related increases in relative kidney and liver weights at higher exposures.

Reliability : (2) valid with restrictions
Study available for review. Pre-guideline, non-GLP study. Limitations in design and reporting but supports overall hazard assessment.

25.11.2003 (10)

Type : Sub-chronic
Species : rat
Sex : male/female
Strain : Fischer 344
Route of admin. : gavage
Exposure period : 13 wk
Frequency of treatm. :
Post exposure period :
Doses : 0, 1.5, 3, 6, 12 or 25 mg/kg bwt/d
Control group :
Method :
Year :
GLP : yes
Test substance : other TS

Remark : Information available from the NTP website indicated that the sub-chronic toxicity of allyl alcohol has been investigated in F-344 rats following gavage administration (NTP study No. C93009). No published report is currently available. This information is included in this set of Robust Summaries for completeness.

25.11.2003 (34)

Type : Sub-chronic
Species : mouse
Sex : male/female
Strain : B6C3F1
Route of admin. : gavage
Exposure period : 13 wk

Frequency of treatm.	:	
Post exposure period	:	
Doses	:	0, 3, 6, 12, 25 or 50 mg/kg bwt/d
Control group	:	
Method	:	
Year	:	
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Remark : Information available from the NTP website indicated that the sub-chronic toxicity of allyl alcohol has been investigated in B6C3F1 mice following gavage administration (NTP study No. C93009). No published report is currently available. This information is included in this set of Robust Summaries for completeness.

25.11.2003 (34)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Bacterial reverse mutation assay
System of testing	:	Salmonella typhimurium TA1535, TA1537, TA1538, TA98 and TA100
Test concentration	:	10-500 ug/plate
Cycotoxic concentr.	:	500 ug/plate
Metabolic activation	:	with and without
Result	:	positive
Method	:	
Year	:	1980
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Method : Tester strains TA1535, TA1537, TA1538, TA98 and TA100 were used with or without S9 from Arochlor 1254 treated rats or hamsters. [Comment: Hamster S9 was used whenever the test compound was not mutagenic with rat S9.]

Testing was conducted using plate incorporation or liquid pre-incubation (45 min at 37 degrees C) methodology, with independent repeat.

Sodium azide, 9-aminoacridine, 2-nitrofluorene and 2-aminoanthracene were used as positive controls (all tester strains, with or without rat and hamster S9).

A compound was considered mutagenic if the number of revertants was twice the background, and a dose-response curve was demonstrable.

Result : Allyl alcohol was mutagenic only in TA1535 in the liquid pre-incubation test, with distilled water as solvent in the presence of hamster S9.

Representative results from one repeat (other not reported):

	Revertants/plate	
Dose (ug)	-S9	+S9
0 (water)	16	22
10	14	38
25	21	37
50	15	55+
75	10	62+
100	17	62+
125	15	64+

175	5	81+
200	10	71+
300	10	55+
500	T	21

+ value at least twice control mean
T toxic

Cytotoxicity was apparent at 500 ug in the plate incorporation test but not at this concentration in the liquid preincubation test.

A satisfactory response was obtained with the positive control substances.

Test substance : Allyl alcohol, >95%, Aldrich Chemical Company (no further details).

Conclusion : Under the conditions of the test, a positive response was obtained with TA1535 in a liquid preincubation assay (negative with plate incorporation) in the presence of hamster S9 (negative in the presence of rat S9, negative in absence of S9). No mutagenic response was seen with TA1537, TA1538, TA98 or TA100.

Reliability : (2) valid with restrictions
Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

22.10.2003 (26)

Type : Bacterial reverse mutation assay
System of testing : Salmonella typhimurium TA100
Test concentration : up to 0.15 umol/2 ml incubation (equivalent to approx. 9 ug/2 ml)
Cycotoxic concentr. : <50% survival at 0.075 umol/2 ml incubation (approx. 4.5 ug/2 ml)
Metabolic activation : with and without
Result : positive
Method :
Year : 1982
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Method : Tester strain TA100 was used in a liquid pre-incubation assay (tightly closed screw-capped vials, 37 degrees C, shaking, 90 min) in the absence and presence of S9 (source not specified). An aliquot from each incubation was diluted and plated onto histidine-containing medium. Mutation frequencies were determined as the number of revertants per umol allyl alcohol. The assay was conducted with an independent repeat.

The concentration range used is not stated. Graphical data indicate that 5 concentrations up to 0.15 umol per 2 ml liquid incubation were employed. Based upon a molecular weight of 58.08, this equates to approx. 9 ug.

Sodium azide was used as positive control in the absence of S9, and 2-aminoacridine in the presence of S9.

Remark : The authors note that <1 ppm acrolein was present in sample of allyl alcohol used in these studies. Concurrent data on acrolein, also included in this publication, lead them to conclude that acrolein (at this concentration) would not have contributed to the mutagenic response observed.

The authors suggest that conversion of allyl alcohol to

acrolein by bacterial alcohol dehydrogenase(s) may account for the strong positive response obtained.

Result : Graphical data demonstrate a clear inverse correlation between survival and induction of revertants in TA100 in the absence of S9.

In the absence of S9, there was a linear increase in the number of revertants per plate over a concentration range of approx. 0.04-0.15 umol/2 ml (equivalent to approx. 2-9 ug).

Survival was also decreased in the presence of S9 (weak mutagenic response), however this effect was considerably less pronounced than was seen in the presence of S9.

A mutation frequency of 750 revertants/umol (approx. 13 revertants/ug) was obtained in the absence of S9, and 145 revertants/umol (approx. 2 revertants/ug) in its presence.

Test substance : Allyl alcohol, 99.9% pure by GC analysis, Merck, Darmstadt, Germany

Conclusion : Under the conditions of the test, a positive response was obtained with TA100 in a liquid preincubation assay in absence of rat S9 (negative in the presence of S9).

Reliability : (2) valid with restrictions
Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

22.10.2003 (29)

Type : Bacterial reverse mutation assay
System of testing : Salmonella typhimurium TA100, TA1535, TA97, TA98
Test concentration : 0.3-166 ug/plate or 3-333 ug/plate
Cycotoxic concentr. : 333 ug/plate
Metabolic activation : with and without
Result : negative
Method : other: US-NTP standard protocol
Year : 2003
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Remark : Only limited information is available for this study which was conducted in the absence or presence of 10% or 30% rat or hamster S9 using a preincubation protocol.

It was run with an independent repeat.

DMSO was the vehicle control with (currently unspecified) positive controls for each strain.

Test substance : Described as allyl alcohol; no further information available.

Conclusion : Under the conditions of the test, no mutagenic activity was detected in 4 strains of Salmonella typhimurium (including TA100 and TA1535) in the absence or presence of rat or hamster S9.

Reliability : (2) valid with restrictions
GLP compliant, NTP guideline study but only limited information available for review, hence Reliability 2.

03.05.2005 (34)

Type : Bacterial reverse mutation assay
System of testing : Salmonella typhimurium TA1535, TA1537, TA1538, TA98, TA100
Test concentration : 0.025, 0.05, 0.10 ul/plate
Cycotoxic concentr. : >0.10 ul/plate

Metabolic activation	:	with and without
Result	:	negative
Method	:	
Year	:	1981
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Method :

SPOT TEST
The ability of allyl alcohol (0.05 ul) to induce reversion in Salmonella typhimurium tester strains TA1535, TA1537, TA1538, TA98, TA100 was investigated using a spot test in the absence or presence of S9 (SD rat, Arochlor 1254 induction). The authors state that the system used was suitable for testing volatile substances. Ethyl methansulfonate (5 ul/plate; TA1535), 9-aminoacridine (10 ug/plate; TA1537), 4-nitro-o-phenyldiamine (10 ug/plate; TA1538 and TA98), methyl methansulfonate (1 ul/plate; TA100) were used as positive control substances in the absence of S9. 2-aminoanthracene (1 ug/plate) was used as positive control substance for all tester strains in the presence of S9.

PLATE INCORPORATION ASSAY
Mutagenic activity was also investigated in TA1535, TA100 and TA98 using a plate incorporation assay and 0.025, 0.05, 0.1 ul allyl alcohol/plate in the absence or presence of S9.

Comment: Concentrations in excess of 0.05 ul (= 50 nl; spot test) or 0.10 ul (= 100 nl; plate incorporation assay) were cytotoxic (no data presented).

Result :

SPOT TEST
The number of his+ revertants per plate was highly comparable in control and test cultures for all 5 tester strains both in the absence or presence of S9. A satisfactory response was obtained with the positive control substances.

PLATE INCORPORATION ASSAY
There was no increase in revertants in any of the 3 tester strains in the absence or presence of S9.

Test substance : Allyl alcohol, analytical grade, Fluka AG (no further details).

Conclusion : Under the conditions of the test, allyl alcohol (highest non-toxic concentration) was not mutagenic in a spot test (5 stains of Salmonella typhimurium including TA100 and TA1535) or a plate incorporation assay (3 tester strains).

Reliability : (2) valid with restrictions
Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

03.05.2005 (36)

Type	:	Bacterial forward mutation assay
System of testing	:	Streptomyces coelicolor, resistance to streptomycin
Test concentration	:	2-100 ul/plate
Cycotoxic concentr.	:	>100 ul/plate
Metabolic activation	:	without
Result	:	negative
Method	:	
Year	:	1981
GLP	:	no

Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Forward mutation of S. coelicolor to streptomycin resistance was investigated in a spot test (100 ul/test) or a plate incorporation assay (2-100 ul/plate). The test medium was supplemented with 1.5 ug/ml streptomycin and approx. 2X10^7 spores (method: Carere et al. (1978) Chem Biol Interact 22, 297-308; Carere et al. (1987) Mut Res 57, 277; no further details.) Ethyl methansulfonate (2 ul/plate) was used a positive control substance.
Result	:	Allyl alcohol was ineffective at inducing mutants in both the spot test and the plate incorporation test. An acceptable response was obtained with the positive control substance.
Test substance	:	Allyl alcohol, analytical grade, Fluka AG (no further details).
Conclusion	:	Under the conditions of the test, allyl alcohol (100 ul) did not induce forward mutations in Streptomyces coelicolor in a spot test or a plate incorporation assay.
Reliability	:	(2) valid with restrictions Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

26.04.2005 (36)

Type	:	Mammalian cell gene mutation assay
System of testing	:	V79 cells, 6-thioguanine resistance
Test concentration	:	1 or 2 uM (equivalent to 58 or 116 ng/ml)
Cycotoxic concentr.	:	>2 uM
Metabolic activation	:	no data
Result	:	positive
Method	:	
Year	:	1990
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Growing cultures of V79 cells in complete Williams medium E (WE; containing 10% fetal bovine serum) were exposed to allyl alcohol (1 uM, 2 uM) for 2 hr, transferred to fresh medium for 24 hr, harvested and then reseeded (10^6 cells) into fresh medium for 10 d, with one subdivision. These cells were harvested and divided for assessment of absolute plating efficiency (after 7 d growth in complete WE) and for mutation frequency (3.17x10^5 cells plated in presence of 3 uM 6-thioguanine; 10 d incubation period with one change of medium). Incubations were performed at 37 degrees C in 95% air:5% carbon dioxide and 80% relative humidity. No exogenous metabolic activation was included. No statistical analysis was applied to the data. Comment: The methods indicate that the concentration of fetal bovine serum present in the WE medium varied between 0-10% during exposure to allyl alcohol. The intention was to

investigate the possible protective role of thiol groups on any mutagenic response observed.

Result : A mutation frequency of 14+/-8 mutants/10^6 survivors was reported after exposure to 1 uM allyl alcohol (58 ng/ml), and 37+/-12 after exposure to 2 uM (116 ng/ml; results are mean and SD of 8 plates from a single experiment).

No concurrent control data are reported.

The thiol status of the above incubations is not reported. Other studies described in this paper indicate that the magnitude of any mutagenic response was greatly diminished by inclusion of 10% fetal bovine serum in the assay. It is therefore assumed that no fetal bovine serum was present.

The authors conclude that allyl alcohol was mutagenic in v79 cells in vitro.

Test substance : Allyl alcohol, Aldrich Chemical Co., Milwaukee, WI (no further details).

Conclusion : Under the conditions of the assay, allyl alcohol was reported to be mutagenic in V79 cells in the absence of exogenous metabolic activation.

Reliability : (4) not assignable
Study available for review. Briefly reported methods and findings, insufficient for full assessment, reliability cannot be assessed.

26.04.2005 (41)

Type : other: fungal point mutation
System of testing : Aspergillus nidulans
Test concentration : 10-40 ul/plate
Cycotoxic concentr. : >40 ul/plate
Metabolic activation : without
Result : negative
Method :
Year : 1981
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : The induction of point mutations in Aspergillus nidulans (haploid strain 35), as detected by resistance to 8-azaguanine, was investigated using a spot test (20 ul allyl alcohol/test) or a plate incorporation assay (10, 20 or 40 ul allyl alcohol/plate). (Method: Bignami et al. (1980) Chem Biol Interact 30, 9; no further details.)

Methyl methansulfonate (1 ul/plate) was used a positive control substance.

Result : Allyl alcohol was ineffective at inducing mutations in both the spot test and the plate incorporation test.

An acceptable response was obtained with the positive control substance.

Test substance : Allyl alcohol, analytical grade, Fluka AG (no further details).

Conclusion : Under the conditions of the test, allyl alcohol (100 ul) did not induce point mutations in Aspergillus nidulans in a spot test (20 ul allyl alcohol/test) or a plate incorporation assay (up to 40 ul/plate).

Reliability : (2) valid with restrictions
Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and

results, suitable for assessment.

26.04.2005 (36)

Type	:	Bacterial reverse mutation assay
System of testing	:	Salmonella typhimurium TA1535, TA1537, TA98 and TA100 Escherichia coli WPuvrA (PKM101)
Test concentration	:	5.0-200 ug/plate (TA1535, TA1537, TA98 and TA100 ±S9 mix) 100-5000 ug/plate (WP2 uvrA (pKM101) -S9 mix) 50-2500 ug/plate (WP2 uvrA (pKM101) +S9 mix)
Cycotoxic concentr.	:	200 ug/plate (TA1535, TA1537, TA98 and TA100 ±S9 mix) 5000 ug/plate (WP2 uvrA (pKM101) -S9 mix) 2500 ug/plate (WP2 uvrA (pKM101) +S9 mix)
Metabolic activation	:	with and without
Result	:	negative
Method	:	other: OECD Guideline 471. Bacterial Reverse Mutation Assay, and USEPA Health Effects Test Guideline OPPTS 870.5100. Bacterial Reverse Mutation Test.
Year	:	2004
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : Tester strains TA1535, TA1537, TA98 and TA100 were used with or without S9 prepared from phenobarbital/ß-naphthoflavone-induced Sprague-Dawley treated rats

Testing was conducted using the standard plate methodology, with independent repeat.

Sodium azide (NaZ), Acridine Mutagen ICR 191 (ICR), Daunomycin HCL (DR), N-Ethyl-N'-nitro-N-Nitrosoguanidine (ENNG) were used as positive controls for tester strains TA100 and TA1535, TA1537, TA98, and WP2 uvrA(pKM101), respectively, without rat S9).

2-aminoanthracene (2AA) and Benzo[a]pyrene (BP) were used as positive controls for all Salmonella tester strains and WP2 uvrA(pKM101), respectively, with rat S9).

DMSO was used as the vehicle control for all tests.

A compound was considered mutagenic when one or both of the following criteria were met:
a) a significant, dose-related increase in the mean number of revertants was observed;
b) a two-fold or greater increase in the mean number of revertant colonies (over that observed for the concurrent solvent control plates) was observed at one or more concentrations.

Result : In at least two separate assays with each tester strain, allyl alcohol did not induce any significant, reproducible increases in the observed number of revertant colonies, either in the presence or absence of S9 mix. The positive controls for each experiment induced the expected responses indicating the strains were responding satisfactorily in each case.

Representative results from one repeat assay (other not reported):

Strain / Compound / Dose (ug) / Mean Revertants per plate			+S9	-S9
TA100:				
	AA	200	0.3	1.7
		100	63.3	83.3

		50	132.7	76.3
		20	156.3	98.3
		10	124.7	86.3
		5	139.3	105.3
	DMSO		142.6	115.4
	2AA	1	2136	
	NaZ	2		1004.0

Strain / Compound / Dose (ug) / Mean Revertants per plate

			+S9	-S9
TA1535:				
	AA	200	0.0	0.0
		100	1.3	0.0
		50	8.7	4.3
		20	9.7	3.0
		10	10.3	9.3
		5	8.7	8.0
	DMSO		14.0	13.7
	2AA	2	287.3	
	NaZ	2		707.3

Strain / Compound / Dose (ug) / Mean Revertants per plate

			+S9	-S9
TA1537:				
	AA	200	0.0	8.0
		100	1.3	16.0
		50	9.3	13.7
		20	12.3	15.0
		10	21.3	15.7
		5	21.7	10.7
	DMSO		19.4	14.0
	2AA	2	318.3	
	ICR	2		382.7

Strain / Compound / Dose (ug) / Mean Revertants per plate

			+S9	-S9
TA98:				
	AA	200	0.0	0.0
		100	1.7	15.0
		50	7.3	20.0
		20	17.7	23.3
		10	28.0	19.7
		5	36.0	32.3
	DMSO		34.5	29.0
	2AA	1	2765.7	
	DR	1		997.3

Strain / Compound / Dose (ug) / Mean Revertants per plate

			+S9	-S9
WP2 uvrA (PKM101):				
	AA	2500	31.7	301.0
		1000	223.0	262.7
		500	331.7	294.3
		200	413.3	217.3
		100	410.0	235.7
		50	388.0	212.3
	DMSO		272.4	200.6
	BP	5	725.7	
	ENNG	1		884.7

Test substance : Allyl alcohol, 99.5%, Sigma-Aldrich
Conclusion : Under the conditions of the assay, allyl alcohol gave a negative, i.e. non-mutagenic, response in S. typhimurium strains TA1535, TA1537, TA98 and

TA100 and E. coli strain WP2 uvrA (pKM101) in both the presence and absence of S9 mix.

Reliability : (1) valid without restriction
Guideline, GLP study. No circumstances occurred that would have affected the quality and integrity of the data.

03.05.2005 (5)

Type : Mammalian cell gene mutation assay
System of testing : Mouse Lymphoma Cells L5178Y
Test concentration : 5-40 ug/mL (with S9 mix)
50-581 ug/mL (without S9 mix)

Cycotoxic concentr. : 30 ug/mL (with S9 mix)
581 ug/mL (without S9 mix)

Metabolic activation : with and without
Result : positive
Method : other: OECD Guideline 476. In Vitro Mammalian Cell Gene Mutation Test; EU Annex V to Council Directive 67/548/EEC published in the 26th Adaptation, Commission Directive 2000/32/EC of May 19, 2000, OJ L136 8.6.2000. B17: In Vitro Mammal
Year : 2004
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Mouse lymphoma L5178Y TK+/- 3.7.2.c cells were used with or without S9 mix prepared from phenobarbital/ ß-naphthoflavone-induced Sprague-Dawley treated rats.

Benzo[a]pyrene (BP) and ethylmethanesulphonate (EMS) were used as positive controls in tests with and without S9 mix, respectively.

DMSO was used as the vehicle control for all tests.

Two series of exponentially growing suspension cultures of L5178Y cells were treated in duplicate with the solvent control, positive controls, or a range of concentrations of allyl alcohol for 4 hours in the presence and absence of S9 mix. The cells were then cultured to allow any induced mutations to be expressed. During this expression time the growth rate was monitored and, where appropriate, the cells subcultured daily. At the end of the 48 hour expression time, samples were grown in both selective and non-selective medium, and the results obtained were used to determine the mutant frequency per viable cell.

The effect of allyl alcohol on the pH and osmolality of the treatment medium was evaluated.

Cell survival was measured by relative total growth. Relative total growth is a measure of growth of test cultures both during the two-day expression and cloning phases of the assay, relative to the vehicle control.

Cell growth in individual microwell plates was assessed after 10-13 days using a dissecting microscope. The survival plates and viability plates were scored for the number of wells containing no cell growth (negative wells). The mutation plates were scored so that each well contained either a small colony (considered to be associated with clastogenic effects), a large colony (considered to be associated with gene mutation effects), or no colony.

The data were evaluated by logit regression, using a complimentary log-log link function. The dependent variable was the number of empty wells. This procedure provided maximum likelihood estimates of log mutant

frequencies. Variances were inflated by the between duplicate heterogeneity factor. Intergroup comparisons of log mutant frequency comparing each treated group with the solvent control were performed within each experiment. All tests were one-sided. Similar analyses were carried out separately for the positive controls.

For a positive response, a statistically significant dose-related increase in mutant frequency was required, but not only at concentrations elliciting high levels of toxicity. An associated absolute increase in mutant number above the solvent control values was a further requirment. Such a response must be reproducible in an independent experiment for the test substance to be described as positive in the assay.

Result : Survival Data
The maximum concentation tested in the absence of S9 mix was 581 ug/mL. This concentration was approximately equivalent to 10mM and as such is the limit concentration for this assay. This concentration resulted in survival levels relative to the solvent control of 103% and 113% in the first and second experiments respectively. In the presence of S9 mix, the maximum concentrations evaluated for mutant frequency were 20 ug/mL and 30 ug/mL giving survival levels of 40% and 11% in the first and second experiments respectively. Treatment of the culture medium with concentrations of test substance used in the study had no significant effect on osmolality or pH.

Mutation Data
No statistically or biologically significant increases in mutant frequency compared to the solvent control cultures, were observed in cultures treated with allyl alcohol at any concentration tested in the absence of S9 mix. In the presence of S9 mix, dose-related increases in mutant frequency were observed in both experiments. These increases achieved statistical significance at the higher concentrations in both experiments and were generally associated with increases in mutant numbers. The positive controls induced appropriate increases in mutant frequency in all mutation experiments, demonstrating the activity of the S9 mix and that the assay was performing satisfactorily.

Representative results from one repeat assay (Experiment 2):

Without S9 Mix:

Compound / Dose (ug/mL) / Mean % Day 0 Rel Survival / Mutant Frequency x 10E-04

AA	581	113	1.8
	400	74	1.7
	200	132	1.1
	100	134	1.2
	50	120	1.4
DMSO	10 (uL/mL)	100	1.3
EMS	500	51	12.0 **

With S9 Mix:

Compound / Dose (ug/mL) / Mean % Day 0 Rel Survival / Mutant Frequency x 10E-04

AA	40	9	#
	30	11	6.9**
	25	26	3.7**
	20	25	3.2**
	15	43	2.0*
	10	66	1.2

	5	59	1.8*
DMSO	10 (uL/mL)	92	1.3
		100	1.2
BP	1	39	6.1*

= not counted due to excessive toxicity
* = P< 0.05
** = P < 0.01

Test substance : Allyl alcohol, >99.9%, Sigma-Aldrich
Conclusion : Under the conditions of the assay, allyl alcohol was mutagenic in L5178Y TK +/- cells treated in vitro in the presence of S9-mix.
Reliability : (1) valid without restriction
Guideline, GLP study. No circumstances occurred that would have affected the quality and integrity of the data.

03.05.2005 (9)

Type : Chromosomal aberration test
System of testing : Human lymphocytes
Test concentration : 25-200 and 100-581 ug/mL (with S9 mix)
100-581 ug/mL (without S9 mix)

Cycotoxic concentr. : 581 ug/mL
Metabolic activation : with and without
Result : positive
Method : other: OECD Guideline 473. In Vitro Mammalian Chromosome Aberration Test and EU Annex V to Council Directive 67/548/EEC published in the 26th Adaptation, Commission Directive 2000/32/EC of May 19, 2000, OJ L136 8.6.2000. B10: In Vitro
Year : 2004
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Human lymphocytes were obtained from blood samples collected on the days of culture initiation from healthy non-smoking donors previously established to have a low incidence of chromosomal aberrations in their peripheral blood lymphocytes.

Cyclophosphamide and Mitomycin C were used as positive controls in tests with and without S9 mix, respectively.

DMSO was used as the solvent control for all tests

Human peripheral blood lymphocytes were used with or without S9 mix prepared from phenobarbital/ ß-naphthoflavone-induced Sprague-Dawley treated rats.

Duplicate human peripheral blood cultures were exposed to the vehicle, test substance or positive control substances at appropriate concentrations in the following experiments:
a) A cytogenetic experiment was conducted using a sample of pooled blood. Cells were exposed to the test substance and control substances for a period of 3 hours, both in the presence and absence of S9 mix. Vehicle, untreated, and positive control cultures were included.
b) A second independent cytogenetic experiment was conducted using a sample of pooled blood. Cells were exposed to the test substance and control substances for a period of 3 hours, both in the presence and absence of S9 mix. Vehicle, untreated, and positive control cultures were included.

Treatment of the cultures started approximately 48 hours after culture initiation. A single sampling time, 20 hours after the start of treatment (68 hours after culture initiation), was used. The OECD guideline for this assay

recommended a period equivalent to about 1.5 cell cycles between the start of treatment and sampling. The sampling time of 20 hours after the start of treatment, used in this study, was based on a measured mean cell cycle time for cultured human peripheral lymphocytes established in the laboratory of 13.5 hours.

The effect of allyl alcohol on pH and osmolality of the culture medium was evaluated using single cultures containing medium only. The solubility of the test substance in the treated blood cultures and in media only cultures was assessed immediately after treatment and at the end of the treatment period.

Slides were examined to determine that they were of suitable quality and, where appropriate, the mitotic index was determined by examining 1000 lymphocytes per culture and calculating the percentage of cells in metaphase. For each experiment, both in the presence and absence of S9 mix, duplicate cultures treated with allyl alcohol at three concentrations were selected for chromosomal aberration analyses along with the appropriate vehicle and positive control cultures. The slides were coded prior to analysis and one hundred cells in metaphase, where possible, were analyzed from each selected culture for the incidence of structural chromosomes.

The percentage of aberrant metaphases and the number of aberrations per cell were calculated for each treatment scored, both including and excluding cells with only gap-type aberrations.

The Fisher Exact Probability Test (one-sided) was used to evaluate statistically the percentage of metaphases showing aberrations (excluding cells with only gap-type aberrations). Data from each treatment group, in the presence and absence of S9 mix, were compared with the respective control group value. A positive response was concluded for an increase in the percentage of aberrant cells, at least at one concentration, which was substantially greater than the laboratory historical solvent control values.

Result **:** The highest concentrations selected for chromosomal aberration analyses were the limit concentration for the assay (581 ug/mL; 10mM) or limited by cytotoxic effects on the chromosomes (200 ug/mL). Concentrations above this were not suitable for analysis due to excessive cytotoxic effects on the chromosomes. Reductions in mean mitotic activity, compared to the solvent control values, were observed in cultures from Experiment 1 (37% +S9 mix) and experiment 2 (23%, + S9 mix; 16% - S9 mix) treated with the highest concentrations of allyl alcohol selected for chromosomal aberration analysis. No reduction in mitotic activity was observed in Experiment 1 in the absence of S9 mix.

Treatment of the culture medium with allyl alcohol up to 581 ug/mL (10mM) had no significant effect on osmolality or pH.

Statistically and biologically significant increases in the percentage of aberrant cells, compared to the vehicle control values, were recorded in cultures from Experiment 1 in the presence of S9 mix and treated in cultures from Experiment 2 in the presence and absence of S9 mix. The positive control materials induced statistically and biologically significant increases in the percentage of aberrant cells, compared to the vehicle control cultures.

Results from Experiment 1 and 2

Without S9 Mix

Compound	Dose (ug/mL)	Mean % Aberrant Cells (excluding gaps)	Mean % Mitotic Index

AA	581	1.00	13.3
	581	12.5**	11.5
	400	1.00	11.7
	400	16.80**	11.5
	100	1.00	15.2
	100	7.50	11.9
DMSO	10 (uL/mL)	0.00	11.1
	10 (uL/mL)	4.00	13.7
Mitomycin C	0.5	23.00**	10.9
	0.5	40.00**	6.8

With S9 Mix

Compound	Dose (ug/mL)	Mean % Aberrant Cells (excluding gaps)	Mean % Mitotic Index
AA	581	10.50**	6.9
	200	18.00**	9.2
	400	3.50	9.3
	100	7.00*	13.0
	100	3.50	12.4
	25	3.00	16.1
DMSO	10 (uL/mL)	2.00	11.0
	10 (uL/mL)	2.00	11.9
Cyclophosphamide	50	32.00**	5.1
	50	48.00**	12.4

* Statistically significantly increase in the percentage of aberrant cells at p< 0.05 using Fisher's Exact Test (one-sided).
** Statistically significantly increase in the percentage of aberrant cells at p< 0.01 using Fisher's Exact Test (one-sided).

Test substance : Allyl alcohol, >99.9%, Sigma-Aldrich
Conclusion : Under the conditions of the assay, allyl alcohol was clastogenic to cultured human lymphocytes treated in vitro in the presence and absence of S9 mix.
Reliability : (1) valid without restriction
Guideline, GLP study. No circumstances occurred that would have affected the quality and integrity of the data.

03.05.2005 (13)

5.6 GENETIC TOXICITY 'IN VIVO'

Type : Cytogenetic assay
Species : rat
Sex : male
Strain : Fischer 344
Route of admin. : i.p.
Exposure period : 72 hr
Doses : 0, 5, 10, 20, 40, 60 or 80 mg/kg bw
Result : negative
Method : other: US-NTP standard protocol
Year : 2001
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : ANIMALS AND TREATMENTS
Male F344 rats were given allyl alcohol at 5, 10 or 20 mg/kg bw (n=5/treatment) by i.p. injection on 3 consecutive days. The control group (n=4) received physiological saline. Bone marrow was collected 24 hr after the final treatment. Two

thousand polychromatic erythrocytes were examined microscopically and scored for the presence of micronuclei. No further experimental details available.

POSITIVE CONTROL SUBSTANCE
Cyclophosphamide (7.5 mg/kg bw) was used as positive control (presumed i.p. injection on 3 consecutive days, however no details available).

STATISTICAL METHODS
Control versus test comparisons are reported together with trend analysis, however no information on methods applied.

Result : There was no statistically significant difference in the number of micronuclei per 1000 PCEs in rats given allyl alcohol at 5, 10 or 20 mg/kg bw/d by i.p. injection on 3 consecutive days:
Control 1.4 MN/1000 PCE
5 mg/kg 2.0
10 mg/kg 1.6
20 mg/kg 1.4
The trend for incidence of micronucleated NCEs was non-significant.

Animals given 40, 60 or 80 mg/kg died prior to scheduled study termination.

A satisfactory response was obtained with the positive control group (24.2 MN per 1000 PCEs; P=0.0000).

Test substance : Allyl alcohol, CAS No 107-18-6, aliquot no. A98432 (no further details).

Conclusion : Under the conditions of the study, no increase in micronucleated polychromatic erythrocytes was detected in male F344 rats given allyl alcohol at doses of up to 40 mg/kg bw/d for three consecutive days.

Reliability : (2) valid with restrictions
GLP compliant, NTP guideline study but only limited information available for review, hence Reliability 2.

16.11.2003 (34)

Type : Cytogenetic assay
Species : mouse
Sex : male/female
Strain : B6C3F1
Route of admin. : gavage
Exposure period : 13 wk
Doses : 0, 3, 6, 12, 25 or 50 mg/kg bw/d
Result : negative
Method : other: US-NTP standard protocol
Year : 2001
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : ANIMALS AND TREATMENTS
Male and female B6C3F1 mice (n=10/sex/dose level for solvent control and treatment groups) were given allyl alcohol at doses of 0, 3, 6, 12, 25 or 50 mg/kg bw/day by oral gavage for 13 weeks. (Comment: the control solvent vehicle is not identified; it is not stated if treatment continued 5 days/week or 7 days/week). Peripheral blood was collected 24 hours after the final treatment. One thousand normochromic erythrocytes were examined microscopically and scored for the presence of micronuclei. No further experimental details available.

POSITIVE CONTROL SUBSTANCE
No positive control substance was used.

STATISTICAL METHODS
Control versus test comparisons are reported together with trend analysis, however no information on methods applied.

Result : There was no statistically significant difference in the number of micronuclei per 1000 NCEs at any treatment level in either sex:
- males
Control 1.1 MN/1000 NCE
3 mg/kg 1.2
6 mg/kg 1.7
12 mg/kg 1.4
25 mg/kg 1.2
50 mg/kg 1.6

- females
Control 0.7 MN/1000 NCE
3 mg/kg 0.9
6 mg/kg 1.0
12 mg/kg 0.7
25 mg/kg 1.5
50 mg/kg 1.1
The trend for incidence of micronucleated NCEs was non-significant.

Test substance : Allyl alcohol, CAS No 107-18-6, aliquot no. A98432 (no further details).

Conclusion : Under the conditions of the study, no increase in micronucleated normochromatic erythrocytes was detected in male or female B6C3F1 mice given allyl alcohol by gavage at doses of up to 50 mg/kg bw/d for 13 weeks.

Reliability : (2) valid with restrictions
GLP compliant, NTP guideline study but only limited information available for review, hence Reliability 2.

03.05.2005 (34)

Type : other: enhanced dominant lethal test (with karyotypic evaluation)
Species : rat
Sex : male
Strain : Sprague-Dawley
Route of admin. : gavage
Exposure period : 33 wk
Doses : 25 mg/kg bw
Result : negative
Method : other: research investigation
Year : 1990
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : ANIMALS AND TREATMENTS
Male SD rats (9-11 wk old) were given 0.85% saline (control group; n=6) or allyl alcohol (25 mg/kg bw/d) by oral gavage (10 ml/kg bw; 7 d/wk for 12 wk, 5 d/wk to wk 15).

Each male was caged with 2 virgin females (until a sperm-positive smear was obtained; up to 6 nights) on wk 1-11.

After mating was complete the males were subject to a gross postmortem examination and hematological screen. Sperm parameters were also assessed (no further methodological

details). Males treated with allyl alcohol were sacrificed in wk 15, while controls were maintained until wk 33 (dosed 5 d/wk, in support of a parallel experiment).

REPRODUCTION PARAMETERS
On GD20, females from mating weeks 1-11 were killed and the uteri examined for:
- total number of corpora lutea
- total implants
- live / dead fetuses
- late / early deaths (calculated as a percentage of the total implants from the pregnant females in each group)

FETAL EXAMINATION
Each fetus was weighed and examined. Abnormal fetuses were photographed (polaroid) prior to removal of a sample of liver (chromosomal preparation) and preservation for skeletal staining and evaluation. The abnormal fetal index was calculated as a percentage of the total number of term fetuses observed at post-mortem. When karyotype abnormalities were observed the chromosome(s) involved were identified according to the standard karyotype of the Norway rat (Committee for a Standardised Karyotype of Rattus norvegicus; not included in study bibliography). (No further details are given on methods used for chromosomal and karyotypic analysis.)

STATISTICAL METHODS
Litter data were analyzed using Fisher's exact test. Other data were evaluated for significant differences relative to the controls, however the methods used are not reported.

Remark : The authors note that paternal exposure to a mutagenic agent result in changes in chromosomal structure and/or number, which may be manifest as fetal abnormalities or changes in karyotype.

Cyclophosphamide (3.5-5.1 mg/kg for up to 33 wk) was also evaluated in this study. It was associated with a highly significant and consistent increase in the numbers of malformed fetuses with karyotypic abnormalities. These effects were paralleled by a large increase in the number of post-implantation losses (dominant lethal events), but no significant effect on sperm parameters. These findings validate the methods used in this study.

Result : PATERNAL EFFECTS
Mean body weight was lower in male rats given allyl alcohol (569+/-49 g) compared to controls (635+/-74g); this may, in part, have reflected the 18 wk age difference at sacrifice. Relative liver weight was increased 26% ($P<0.05$), and relative spleen weight 22% ($P<0.05$), with non-significant increases in relative kidney and testis weights (data not reported).

Red cell count, mean cell volume, percentage cell volume and hemoglobin concentration were unaffected by treatment with allyl alcohol (data not reported). White cell counts were similar in treated and control animals, however a differential count revealed a significant increase in percentage of lymphocytes with a corresponding significant decrease in eosinophils and neutraphil counts (data not reported). The authors comment that these changes in differential count were within the normal range for the SD

rat.

Total sperm count and epididymal sperm concentration were unaffected by treatment (data not reported).

REPRODUCTION PARAMETERS
There was a total of 1669 live implants from 125 pregnancies in the controls (13.4 implants/litter) versus 1371 liver implants from 108 litters in the allyl alcohol-treated group (12.7 implants/litter) (non significant).

Mean preimplantation loss was comparable in control (12.8+/-5.4%) and treated (11.7+/-6.2%) groups.

The rate of post-implantation loss (dominant lethality) varied between 2.2-13.2% in the controls, with a mean for the whole study (13 matings) of 6.2%. The comparable range for the male rats given allyl alcohol was 1.7-8.7%, with an overall mean of 4.7%.

FETAL ABNORMALITIES
The incidence of runted, abnormal and grossly abnormal fetuses was comparable in the control and treated groups.

	Control	Treated
Total number runts	13 (0.78%)	13 (0.95%)
Total number gross abnormalities (%)	0 (0%)	3 (0.22%)
Total number abnormal fetuses (%)	13 (0.78%)	16 (1.17%)

The three abnormalities in the treated group comprised were diagnosed as:
- anasarca (massive edema)
- exencephaly
- craniofacial and skeletal abnormality.

The combined incidence of gross abnormalities was not statistically significantly different between the control (n=0) and treated (n=3) groups.
Comment: The authors note that the incidence of grossly abnormal fetuses (0.22%) was within the historic range for this strain of rat (not reported) and were therefore considered to be spontaneous in origin.

KARYOTYPIC ANALYSIS
Karyotypic abnormalities were present in 3 of 12 slides prepared from abnormal fetuses from the treated group whereas no abnormal karyotype was present in 5 slides from the controls:

	Control	Treated
No. of abnormal fetuses evaluated:	8	14
Slides with scorable metaphases:	5	12
Slides with no karyotypic abnormality	5	9
Slides with karyotypic abnormality	0	3

The abnormalities from the allyl alcohol treated group were diagnosed as:
- trisomy with 3 fragments of possible centromeric origin in every metaphase (runt)
- trisomy (anasarca/runt)
- trisomy (craniofacial/skeletal)

Comment: Data for other endpoints described in the methods section are not reported in the paper; it is assumed that these were unaltered by treatment with allyl alcohol.

Test substance	:	Allyl alcohol, Aldrich Chemical Co., Gillingham, Dorset, UK (no further details).
Conclusion	:	Under the conditions of the study, no increase in post-implantation loss (dominant lethality) or chromosomal/karyotypic abnormalities were present in fetuses sired by male SD rats given allyl alcohol at 25 mg/kg bw/d for up to 12 wk.
Reliability	:	(2) valid with restrictions Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods and results, suitable for assessment.

03.05.2005 (23)

5.7 CARCINOGENICITY

Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	drinking water
Exposure period	:	106 wk
Frequency of treatm.	:	
Post exposure period	:	until natural death
Doses	:	0 or 300 mg/l
Result	:	negative
Control group	:	yes, concurrent vehicle
Method	:	
Year	:	1987
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Method :

Male and female F344 rats (n=20/sex; age 7-8 wk; housed 4/cage) were given allyl alcohol (300 mg/l) in drinking water 5 d/wk for up to 106 wk (tap water given on remaining days). A similar number of animals received tap water ad libitum. The animals were allowed to survive until natural death or until wk 123-132 of the study, which ever occurred later.

Fresh solutions were prepared weekly and stored in a refrigerator until use. Stability studies (GC analysis) demonstrated 100% recovery of allyl alcohol after 7 days (no further information available).

No further experimental details available.

Result :

Median survival was unaffected by treatment:
- males: controls = 115 wk, treated = 113 wk
- females: controls = 118 wk, treated = 112 wk

The tumors observed in this study were stated to be of the types commonly seen in untreated F344 rats. Findings were as follows:

LIVER:
Hyperplastic nodules and a few well differentiated hepatocellular carcinoma.
Controls: 2/20 M; 2/20 F
Treated: 3/20 M; 6/20 F

ADRENAL CORTEX:
Hyperplastic nodules and adenoma.

Controls: 1/20 M; 1/20 F
Treated: 0/20 M; 0/20 F

PITUITARY:
No description.
Controls: 14/20 M; 14/20 F
Treated: 10/20 M; 10/20 F

LEUKEMIA:
No description.
Controls: 12/20 M; 6/20 F
Treated: 8/20 M; 6/20 F

Comment: While the authors comment that the occurrence of specific tumor types was increased after treatment with other substances included in this study, the increased occurrence of hepatic nodules/carcinoma in females given allyl alcohol relative to that present in the controls is not the subject of discussion. This suggests this finding was considered of doubtful biological significance.

Test substance : Allyl alcohol, Aldrich Chemical Company (no further details).

Conclusion : Under the conditions of this study, no clear evidence of carcinogenicity was seen in male or female F344 rats given allyl alcohol in drinking water (300 mg/l) for up to 106 wk.

Reliability : (2) valid with restrictions
Study available for review. Non-guideline, non-GLP study. Reasonably well reported methods but limited reporting of results. Supports overall hazard assessment.

04.11.2003 (27)

Species : Syrian hamster
Sex : male
Strain :
Route of admin. : gavage
Exposure period : 60 wk
Frequency of treatm. :
Post exposure period : until natural death
Doses : 0 or 2 mg/day
Result : negative
Control group : yes, concurrent vehicle
Method :
Year : 1987
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Remark : In a poorly reported study, no increase in tumors of the adrenal cortex, forestomach or pancreas duct was noted in male Syrian hamsters give 2 mg allyl alcohol in corn oil for up to 60 wk. The animals were allowed to survive until natural death or for up to a further 30-32 wk post-treatment. Although not stated, it is assumed that gavage administration was employed.

Test substance : Allyl alcohol, Aldrich Chemical Company (no further details).

Reliability : (4) not assignable
Study available for review. Briefly reported methods and findings, insufficient for full assessment, reliability cannot be assessed.

17.10.2003 (27)

5.8.1 TOXICITY TO FERTILITY

Type	:	other
Species	:	rat
Sex	:	male
Strain	:	Wistar
Route of admin.	:	drinking water
Exposure period	:	15 wk
Frequency of treatm.	:	
Premating exposure period		
Male	:	
Female	:	
Duration of test	:	
No. of generation studies	:	
Doses	:	
Control group	:	
Method	:	
Year	:	1978
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Method :

ANIMALS AND TREATMENTS
Groups of Wistar rats (15/sex/treatment level) were exposed to allyl alcohol in the drinking water at 0 (control), 50, 100, 200 or 800 ppm for 15 weeks.

NECROPSY AND HISTOPATHOLOGY
At the end of the appropriate treatment period, animals were killed by exsanguination following an overnight fast and subject to a post-mortem examination. This included gonadal weights and histopathological examination of testis, ovary and uterus.

See Section 5.4 for further experimental details.

Result :

INTAKE OF TEST SUBSTANCE
The calculated mean intake of allyl alcohol over the course of the study (based on body weight and water intake data) was:
Males: 0, 4.8, 8.3, 14.0, 48.2 mg/kg bw/d
Females: 0, 6.2, 6.9, 17.1 and 58.4 mg/kg bw/d

POST MORTEM EXAMINATION
Absolute organ weights (including gonadal weights) were generally decreased in males, and to a lesser extent in females, in a time- and treatment related manner. Relative organ weights (including gonadal weights) were generally increased to a statistically significant extent in high dose animals of both sexes at study termination. These changes appeared secondary to a reduction in water intake (presumably due to unpalatability of the treatment solution) and body weight, that was particularly pronounced in high dose animals.

HISTOPATHOLOGICAL EVALUATION
No histopathological abnormalities were reported for testis, ovary or uterus.

Test substance : Allyl alcohol, 99% pure, SG (20 degree C) 0.849-0.852; bpt 95-98 degrees C, supplied by Bush Boake Allen Ltd, London.

Conclusion : No treatment-related changes were present in gonadal weights or histopathology in male and female rats given allyl

alcohol at received doses of up to 48-58 mg/kg bwt/d.

Reliability : (2) valid with restrictions
Study available for review. Non-guideline, non-GLP study. Reasonably well reported methods and results, suitable for assessment.

04.11.2003 (6)

Type : other
Species : rat
Sex : male
Strain : Sprague-Dawley
Route of admin. : gavage
Exposure period : up to 15 wk
Frequency of treatm. : 7 d/wk
Premating exposure period
Male : up to 11 wk
Female : untreated
Duration of test :
No. of generation studies :
Doses :
Control group :
Method : other: research investigation
Year : 1990
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Method : ANIMALS AND TREATMENTS
Male SD rats (9-11 wk old) were given 0.85% saline (control group; n=6) or allyl alcohol (25 mg/kg bw/d) by oral gavage (10 ml/kg bw; 7 d/wk for 12 wk, then 5 d/wk to wk 15).

Each male was caged with 2 virgin females (until a sperm-positive smear was obtained; up to 6 nights) on wk 1-11.

After mating was complete the males were subject to a gross postmortem examination. Gonadal weights and sperm parameters (no further methodological details) were assessed. Males treated with allyl alcohol were sacrificed in wk 15, while controls were maintained until wk 33 (dosed 5 d/wk, in support of a parallel experiment).

REPRODUCTION PARAMETERS
On GD20, females from mating weeks 1-11 were killed and the uteri examined for:
- total number of corpora lutea
- total implants
- live / dead fetuses
- late / early deaths (calculated as a percentage of the total implants from the pregnant females in each group)

STATISTICAL METHODS
Litter data were analyzed using Fisher's exact test. Other data were evaluated for significant differences relative to the controls, however the methods used are not reported.

Result : PATERNAL EFFECTS
Mean body weight was lower in male rats given allyl alcohol (569+/-49 g) compared to controls (635+/-74g); this may, in part, have reflected the 18 wk age difference at sacrifice.

Relative testis weights were increased (data not reported;

non-significant).

Total sperm count and epididymal sperm concentration were unaffected by treatment (data not reported).

REPRODUCTION PARAMETERS
There was a total of 1669 live implants from 125 pregnancies in the controls (13.4 implants/litter) versus 1371 liver implants from 108 litters in the allyl alcohol-treated group (12.7 implants/litter) (non significant).

Mean preimplantation loss was comparable in control (12.8+/-5.4%) and treated (11.7+/-6.2%) groups.

Comment: Data for other endpoints described in the methods section are not reported in the paper; it is assumed that these were unaltered by treatment with allyl alcohol.

Test substance : Allyl alcohol, Aldrich Chemical Co., Gillingham, Dorset, UK (no further details).

Conclusion : Under the conditions of the study, no statistically significant changes were present in relative testis weight, total sperm count and epididymal sperm concentration or reproductive performance for male SD rats given allyl alcohol at 25 mg/kg bw/d for up to 12 wk.

Reliability : (2) valid with restrictions
Study available for review. Non-guideline, non-GLP experimental study. Reasonably well reported methods but limited reporting of results. Supports overall hazard assessment.

04.11.2003 (23)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	female
Strain	:	other: Crl:CD® (Sprague-Dawley) IGS BR
Route of admin.	:	gavage
Exposure period	:	Gestation day 6 through 19
Frequency of treatm.	:	daily
Duration of test	:	
Doses	:	0, 10, 35, or 50 mg/kg bwt day
Control group	:	yes
NOAEL maternal tox.	:	< 10 mg/kg bw
NOAEL teratogen.	:	= 10 mg/kg bw
LOAEL Maternal Toxicity	:	= 10 mg/kg bw
LOAEL Teratogenicity	:	= 35 mg/kg bw
Method	:	other: EPA Health Effects Testing Guidelines OPPTS 870.3700 and OECD Guideline 414 - Prenatal Developmental Toxicity Study
Year	:	2005
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : ANIMALS AND MAINTENANCE
- Species and strain: rat, Crl:CD (SD)IGS BR (Charles River Laboratories, Raleigh, NC, USA)
- Age: 71 days on receipt
- Acclimation period: 13 days
- Group size: n=25
- Housing: individually housed in suspended wire mesh cages

- Diet: Certified Rodent Lab Diet 5002 (PMI Nutrition International Inc.), ad libitum
- Water: reverse osmosis-treated tap water, ad libitum - Environment: controlled within range of 70.4 to 71.5 degrees F, 41.9 to 53.9 % rel. humidity, 12 hour light/dark cycle, 10 air changes/hour
- age at first treatment: approx. 12-13 weeks

PREPARATION OF DOSING SOLUTIONS
Oral dosing solutions were prepared weekly in deionized water vehicle and stored at room temperature for a period that did not exceed 10 days in duration.

CONTROL
Control group was dosed with deionized water

ANALYSIS OF DOSING SOLUTIONS
An aliquot from each formulation was taken from each weekly preparation and analyzed for concentration verification. Stability was determined over 10 days (room temperature).

CLINICAL OBSERVATIONS
All rats were observed twice daily, once in the morning and once in the afternoon, for moribundity and mortality. Individual detailed clinical observations were recorded from gestation days 0 through 20 (prior to dose administration during the treatment period). Animals were also observed for signs of toxicity at the time of dose administration and approximately 1 hour following dose administration. All significant findings were recorded. Individual maternal body weights were recorded on gestation days 0 and 6-20 (daily). Group mean body weights were calculated for each of these days. Mean body weight changes were calculated for each corresponding interval and also for gestation days 6-9, 9-12, 12-20, 6-20 and 0-20. Gravid uterine weight was collected and net body weight (the day 20 body weight exclusive of the weight of the uterus and contents) and net body weight change (the day 0-20 body weight change exclusive of the weight of the uterus and contents) were calculated and presented for each gravid female at the scheduled laparohysterectomy. Individual feed consumption was recorded on gestation days 0 and 6-20 (daily). Feed intake was reported as g/animal/day and g/kg/day for the corresponding body weight change intervals.

NECROPSY
A gross necropsy was performed on females that died during the course of the study. Representative sections of the liver and all gross lesions were retained in 10% neutral-buffered formalin for possible future histopathologic examination. The number and location of implantation sites and corpora lutea were recorded. All surviving females were euthanized on gestation day 20 by carbon dioxide inhalation. The thoracic, abdominal and pelvic cavities were opened by a ventral mid-line incision, and the contents were examined without knowledge of treatment group. In all instances, the post mortem findings were correlated with the ante mortem comments and any abnormalities were recorded. The uterus and ovaries were then exposed and excised. The number of corpora lutea on each ovary was recorded. The trimmed uterus was weighed and opened, and the number and location of all fetuses, early and late resorptions and the total number of implantation sites were recorded. The placentae were also examined. The individual uterine distribution of implantation sites was documented using the following procedure. All implantation sites, including resorptions, were numbered in consecutive order beginning with the left distal to the left proximal uterine horn, noting the position of the cervix, and continuing from the right proximal to the right distal uterine horn. Liver weights were recorded and representative sections of the liver and all gross lesions were

preserved in 10% neutral-buffered formalin for possible future histopathologic examination. Representative sections of corresponding organs from a sufficient number of control animals were retained for comparison. The carcass of each female was then discarded. Uteri with no macroscopic evidence of implantation were opened and subsequently placed in 10% ammonium sulfide solution for detection of early implantation loss. Intrauterine data were summarized using calculations based on both a 1) Group Mean Litter Basis and 2) Proportional Litter Basis.

EXAMINATION OF THE FETUSES
Each viable fetus was examined externally, individually sexed, weighed, tagged for identification, and euthanized by hypothermia followed by an intrathoracic injection of sodium pentobarbital (if necessary). The detailed external examination of each fetus included, but was not limited to, an examination of the eyes, palate and external orifices, and each finding was recorded. Nonviable fetuses (if the degree of autolysis was minimal or absent) were examined, the crown-rump length measured, weighed, sexed and tagged individually. Crown-rump measurements and degrees of autolysis were recorded for late resorptions, and the tissues were discarded.

Each viable fetus was subjected to a visceral examination using a modification of the Stuckhardt and Poppe (Teratogenesis, Carcinogenesis and Mutagenesis, 4:181-188, 1984) fresh dissection technique to include the heart and major blood vessels. The sex of each fetus was confirmed by internal examination. Fetal kidneys were examined and graded for renal papillae development. Heads from approximately one-half of the fetuses in each litter were placed in Bouin's fixative for subsequent soft-tissue examination by the Wilson sectioning technique. The heads from the remaining one-half of the fetuses were examined by a mid-coronal slice. All carcasses were eviscerated and fixed in 100% ethyl alcohol. Following fixation in alcohol, each fetus was macerated in potassium hydroxide and stained with Alizarin Red S and Alcian Blue. External, visceral and skeletal findings were recorded as developmental variations (alterations in anatomic structure that are considered to have no significant biological effect on animal health or body conformity and/or occur at high incidence, representing slight deviations from normal) or malformations (those structural anomalies that alter general body conformity, disrupt or interfere with normal body function, or may be incompatible with life). The fetal developmental findings were summarized by: 1) presenting the incidence of a given finding both as the number of fetuses and the number of litters available for examination in the group; and 2) considering the litter as the basic unit for comparison and calculating the number of affected fetuses in a litter on a proportional basis as follows:

Summation per Group (%) = summation of Viable Fetuses Affected/Litter (%) divided by No. Litters/Group

Where:
Viable Fetuses Affected/Litter (%) = No. Viable Fetuses Affect./Litter divided by No. Viable Fetuses/Litter x 100

STATISTICAL METHODS
Analyses were conducted using two-tailed tests (except as noted otherwise) for minimum significance levels of 1% and 5%, comparing each test article-treated group to the control group. Each mean was presented with the standard deviation (S.D.) and the number of animals (N) used to calculate the mean. Where applicable, the litter was used as the experimental unit.

Mean maternal body weights (absolute and net), body weight changes

(absolute and net) and feed consumption, gravid uterine weights, numbers of corpora lutea, implantation sites and viable fetuses, and fetal body weights (separately by sex and combined were subjected to a parametric one-way analysis of variance (ANOVA) (Snedecor and Cochran, Statistical Methods, 7th ed.; The Iowa State University Press: Ames, IA, pp 215-237, 1980) to determine intergroup differences. If the ANOVA revealed statistically significant ($p<0.05$) intergroup variance, Dunnett's test (Dunnett, Biometric, 20:482-491,1964) was used to compare the test article-treated groups to the control group. Mean litter proportions (percent per litter) of prenatal data (viable and nonviable fetuses, early and late resorptions, total resorptions, pre- and postimplantation loss, and fetal sex distribution), total fetal malformations and developmental variations (external, visceral, skeletal and combined) and each particular external, visceral and skeletal malformation or variation were subjected to the Kruskal-Wallis nonparametric ANOVA test (Kruskal and Wallis, Journal of the American Statistical Association, 47:583-621,1952) to determine intergroup differences. If the ANOVA revealed statistically significant ($p<0.05$) intergroup variance, the Dunn's test (Dunn, Technometrics, 6(3):241-252,1964) was used to compare the test article-treated groups to the control group.

Result : Maternal Toxicity LOAEL - 10 mg/kg bwt/day, NOAEL - <10 mg/kg bwt/day

Developmental Toxicity LOAEL - 35 mg/kg bwt/day, NOAEL - 10 mg/kg bwt/day

The developmental toxicity observed was limited to an increased frequency of total litter loss in the 35 and 50 mg/kg bwt/day dose levels (2/group). In each instance of total litter loss, the dam experienced severe toxicity (loss of body weight, severe decreases in feed consumption, and evidence of significant liver toxicity). Signs of liver toxicity were noted in dams in the 10 mg/kg bwt/day group. One and six females from the 35 and 50 mg/kg bwt/day groups, respectively, died between gestation days 9 and 20. Despite the severe maternal toxicity observed, there were no test-article related increases in malformation rates or incidence of variations. Intrauterine growth and survival was not affected in the fetuses from dams that survived to necropsy.

SURVIVAL AND CLINICAL SIGNS
One and six females in the 35 and 50 mg/kg bwt/day groups, respectively, were found dead between gestation days 9-20. The following clinical observations were noted within 4 days for all females found dead: salivation and/or clear material on various body surfaces and wiping the mouth on the cage floor and/or walls at the daily examinations and/or 1 hour following dose administration as a result of the irritant properties of the test article, signs of poor grooming as a result of declining health, including unkempt appearance and/or yellow, brown and/or red colored material on various body surfaces, behavioral findings indicative of moribundity, including extremities cool to the touch, rocking, lurching or swaying while walking and/or hypoactivity at the daily examinations and/or 1 hour following dose administration. One female had shallow respiration and several had decreased defecation.

The following findings were noted at necropsy of the animals that died during the dosing period: distended stomach, dark red stomach contents and/or dark red areas on the stomach lining, white and yellow areas on the liver at necropsy, and (in one animal) an entirely resorbed litter. Based on all of the adverse maternal findings in the animals found dead in the 35 and 50 mg/kg bwt/day groups, all mortalities were considered test article-related. All other animals survived to the scheduled necropsy.

At the time of dose administration, salivation was noted in several animals in the 35 and 50 mg/kg bwt/day groups, respectively. Excessive pawing of

and/or mouth wiping on the cage floor and/or walls occurred in many of the animals in the 10, 35 and 50 mg/kg bwt/day groups, respectively, at the time of dosing. However, these findings were rarely observed 1 hour following dose administration. Lacrimation was observed in six females in the 50 mg/kg bwt/day group approximately 1 hour following dose administration. All of these clinical findings were attributed to the irritant properties of the test article. In addition, red, yellow and/or brown materials on various body surfaces were found in six females approximately 1 hour following dose administration in both the 35 and 50 mg/kg bwt/day groups.

BODY WEIGHT AND FEED INTAKE
All animals found dead had large body weight losses and reduced feed consumption within 2-4 days prior to death.

Maternal body weight effects present in the 50 mg/kg bwt/day group included: maternal body weight loss of 12 g during gestation days 6-9 compared to a mean body weight gain of 11 g in the control group. ($p<0.05$) lower maternal body weights on gestation days 8-11 (5.3% to 8.5%) and continued to be slightly reduced (3.6% to 5.5%) throughout the remainder of the treatment period. ($p<0.05$) Because many of the most severely affected animals in this group died by gestation day 11, mean body weight gain in this group was statistically significantly ($p<0.05$) higher on gestation days 9-12 and similar to the control group on gestation days 12-20.

Maternal body weight effects present in the 35 mg/kg bwt/day group included: maternal body weight loss of 4 g during gestation days 6-9 compared to a mean body weight gain of 11 g in the control group. ($p<0.01$) Mean maternal body weight gains in the 35 mg/kg bwt/day group were similar to the control group during gestation days 9-12, but statistically significantly ($p<0.05$ or $p<0.01$) reduced on gestation days 12-20 and when the entire treatment period (gestation days 6-20) was evaluated. The sustained reductions in mean body weight gain in the 35 mg/kg bwt/day group were attributed to the continued survival of the animals most affected by test article administration. This trend was opposite that observed in the 50 mg/kg bwt/day group, where those animals most affected by test article administration died between gestation days 9 and 16, thus no longer contributing to the overall reduced mean body weight gains. As a result of the effects on mean body weight gain in the 35 mg/kg bwt/day group, mean body weights were reduced 4.0% to 7.6% on gestation days 16 to 20; the difference on gestation day 20 was statistically significant ($p<0.05$).

Mean maternal body weights, body weight gains, net body weight, and net body weight gain in the 10 mg/kg bwt/day group were similar to the control group.

FEED CONSUMPTION
A decrease ($p<0.01$) in mean maternal feed consumption, (evaluated as g/animal/day and g/kg bwt/day), was noted for the 50 mg/kg bwt/day group during gestation days 6-9 and 9-12. Mean feed consumption in this group was similar to the control group when the entire treatment period (gestation days 6-20) was evaluated as a result of the deaths of the most severely affected animals by gestation day 16. Mean feed consumption measured as g/kg bwt/day was higher than the control group during gestation days 12-20. However, since mean feed consumption measured as g/animal/day was similar to the control group, this effect was attributed to the reduced body weights in this group.

In the 35 mg/kg bwt/day group, a reduction ($p<0.01$) in mean feed consumption was observed during gestation days 6-9, that corresponded to the reduced mean body weight gain in this group for the same interval. Mean feed consumption was lower ($p<0.05$) on gestation days 9-12. Due to

the mortality observed in this study and the number of animals not consuming an appreciable amount of feed, the staff veterinarian and the sponsor approved administration of supplemental feed (an approximately 50/50 mixture of Hills Prescription Diet canine feed and water) to all animals consuming less than 10 g per day. Reported feed consumption values include only the amount of basal feed consumed and do not include the amounts of supplemental diet administered. Supplementation of the diet with the prescription diet for six animals in the 35 mg/kg bwt/day group beginning on gestation day 14 allowed for mean feed consumption values to increase, albeit not to control values. There was a reduction ($p<0.01$) in mean feed consumption (g/animal/day) noted in the 35 mg/kg bwt/day group when the entire treatment period (gestation days 6-20) was evaluated. Therefore, the lower feed consumption in the 35 mg/kg/day group relative to the 50 mg/kg bwt/day group during gestation days 12-20 and 6-20 was attributed to the continued survival of the most affected animals in the 35 mg/kg bwt/day group due to dietary supplementation.

Feed consumption in the 10 mg/kg bwt/day group was similar to that in the control group throughout gestation. Differences from the control group were slight and not statistically significant.

MATERNAL NECROPSY DATA
One and six females in the 35 and 50 mg/kg bwt/day groups, respectively, were found dead between gestation days 9-20. The one female in the 35 mg/kg bwt/day group had white and yellow areas on all lobes of the liver and an entirely resorbed litter (all early resorptions). Three of the females that died in the 50 mg/kg bwt/day group had a distended stomach, dark red stomach contents, and/or dark red areas on the stomach lining. These stomach findings were attributed to the irritant properties of the test article. All animals found dead had severe mean body weight losses and reduced food consumption within 2-4 days prior to death.

At the scheduled necropsy on gestation day 20, 11 of the surviving 24 and 12 of the surviving 19 females in 35 and 50 mg/kg bwt/day groups, respectively, had test article-related liver findings, including yellow and/or white areas on the liver, liver adhesions and/or misshapen or mottled livers. Of the animals with liver findings, one female each in the 35 and 50 mg/kg bwt/day groups had an enlarged spleen and two females in the 35 mg/kg bwt/day group had a thickened pericardium and/or pericardium adhesions, one of which also had white discoloration of the heart. One female in the 10 mg/kg bwt/day group had yellow areas on the liver. The yellow areas on the liver were considered to be test article-related because this finding was observed at a higher incidence in the 35 and 50 mg/kg bwt/day groups but was not observed in any control group females.

MATERNAL ORGAN WEIGHTS
Test article-related increases in mean liver weights (5.4% and 11.6%) were observed in the 35 and 50 mg/kg bwt/day groups, respectively, when compared to the control group. The increased liver weights correlated with the macroscopic liver findings observed in these two groups. No test article-related effects mean liver weight was noted in the 10 mg/kg bwt/day group.

GESTATION DAY 20 LAPAROHYSTERECTOMY DATA
Test article-related increases (not statistically significant) in the mean litter proportions of postimplantation loss (early resorptions) were observed in the 35 and 50 mg/kg bwt/day groups (16.2% and 14.3% per litter, respectively) compared to the control group value (6.9% per litter). These values also exceeded the maximum value in the laboratory historical control data (8.6% per litter). Corresponding reductions in the mean litter proportion of viable fetuses were also observed in the 35 and 50 mg/kg bwt/day groups. The increased postimplantation loss in these two groups

was primarily attributed to two female rats in each of the 35 mg/kg bwt/day and 50 mg/kg bwt/day groups that had entirely resorbed litters. These animals also had test article-related effects in mean body weight gains during the treatment period. The mean litter proportion of postimplantation loss was unaffected by test article administration in the 10 mg/kg bwt/day group.

Overall mean fetal weight was slightly reduced (3.4 g) in the 35 mg/kg bwt/day group when compared to the control group (3.6 g). However, this was primarily due to one female rat that had a drastically reduced mean fetal weight (1.7 g) and also resorbed 39% of its litter. This dam also had a large body weight loss over the entire treatment period. Due to these factors as well as the lack of a dose response across groups, the reduction in mean fetal weight in the 35 mg/kg bwt/day group was not considered to be a direct effect of test article administration. Mean fetal weight in the 10 and 50 mg/kg bwt/day groups was unaffected by test article administration.

Other parameters evaluated, including mean live litter size, fetal sex ratios and numbers of corpora lutea and implantation sites, were similar to the control group values at all dose levels.

FETAL MORPHOLOGICAL DATA
The numbers of fetuses (litters) available for morphological evaluation were 387(25), 406(24), 296(19) and 241(16) in the control, 10, 35 and 50 mg/kg bwt/day groups, respectively. Malformations were observed in 0(0), 2(2), 1(1) and 0(0) fetuses (litters) in these same respective dose groups and were considered spontaneous in origin. When the total malformations (0.0%, 0.5%, 0.5% and 0.0% per litter) and developmental variations (37.6%, 37.5%, 41.2% and 40.9% per litter) were evaluated on a proportional basis in the control, 10, 35 and 50 mg/kg bwt/day groups, respectively, no statistically significant differences from the control group were noted. Fetal malformations and developmental variations, when observed in the test article-treated groups, occurred infrequently or at a frequency similar to that in the control group, did not occur in a dose-related manner and/or were within the laboratory historical control data ranges. Based on these data, no fetal malformations or developmental variations were attributed to the test article.

Test substance : Allyl alcohol; 99.4%

Conclusion : Maternal toxicity in the 35 and 50 mg/kg bwt/day groups consisted of mortalities, clinical findings, reductions in body weight gain and feed consumption, macroscopic liver findings and increased liver weights. One female in the 10 mg/kg bwt/day group also had macroscopic liver findings. Therefore, a dose level of 10 mg/kg/day was considered to be the lowest-observed-adverse- effect level (LOAEL) for maternal toxicity. Developmental toxicity in the 35 and 50 mg/kg bwt/day groups was expressed by an increase in postimplantation loss. Therefore, a dose level of 10 mg/kg bwt/day was considered to be the no-observed-adverse-effect level (NOAEL) for developmental toxicity when allyl alcohol was administered orally by gavage to pregnant rats.

Reliability : (1) valid without restriction
Guideline, GLP study. No circumstances occurred that would have affected the quality and integrity of the data.

03.05.2005 (43)

Species : rat
Sex : female
Strain : Sprague-Dawley
Route of admin. : other: intraamniotic injection
Exposure period :
Frequency of treatm. :
Duration of test :
Doses :

Control group	:	
Method	:	
Year	:	1985
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Time-mated pregnant SD rats (225-250; Charles River Canada Inc.) were anesthetized (ether) on GD13 and the uteri exposed. Embryos in one uterine horn received an intraamniotic injection (10 ul; 30-gauge needle) of allyl alcohol (10, 100 or 1000 ug/fetus in 0.9% NaCl) while those in the other horn were untreated. An unspecified number of saline injected controls were also included in the study and treated in a similar manner (i.e., injected or sham treated). The uterus was repositioned and the laporotomy closed (nylon sutures). Rats were sacrificed on GD20 (ether overdose) and the number of dead or resorbed fetuses recorded. Live fetuses were examined for external malformations, blotted dry and weighed. The results were analyzed using the Mann-Whitney U-Test.
Result	:	Approx. 24% of the saline-injected control fetuses and 12% of the sham control fetuses were resorbed; 6% or 5%, respectively, were malformed. Comment: The number of control litters is not reported. Allyl alcohol treatment was associated with a dose-related increase in resorptions (treated uterine horn versus untreated contralateral horn), which was significant in the intermediate and high treatment groups. While no tabulated results are available, interpolation from graphical data included in the publication indicates that the mean number of dead or resorbed fetuses was 0.3, 0.5 ($P<0.05$) and 0.6 ($P<0.05$) in the 10 (5 litters), 100 (8 litters) and 1000 (7 litters) ug/fetus groups. Comment: The occurrence of dead or resorbed fetuses also increased in a treatment-related manner in the fetuses from the contra-lateral (untreated) uterine horn : <0.1, 0.2, 0.4 for the low, intermediate and high dose groups. Two fetuses from 7 high dose litters were malformed (limb defects; non-significant). Two contralateral controls (untreated) from 8 intermediate dose litters were also malformed (omphalocele, edema, micromelia of the limbs, clubfoot, short neck and micrognathia; the other had a minor forelimb defect).
Test substance	:	Allyl alcohol, Aldrich Ltd, Montreal, Canada (no further details).
Conclusion	:	A treatment related increase in dead and resorbed fetuses was reported following intraamniotic injection of 100 or 1000 ug allyl alcohol/fetus on GD13. However the non-physiological route of exposure, together with an increased occurrence of dead/resorbed fetuses in the untreated (contra-lateral) uterine horn, suggests these observations are of doubtful reliability for the purposes of hazard identification.
Reliability	:	(4) not assignable Study available for review. Briefly reported methods and findings, insufficient for full assessment, reliability

cannot be assessed.

03.05.2005 (39)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

5.11 ADDITIONAL REMARKS

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

(1) Armstrong, T (2003) Allyl alcohol bioaccumulation model. Unpublished study (modeling) for Lyondell Chemical Co., 17 November 2003.

(2) Armstrong, T (2003) Allyl alcohol fate and transport modeling. Unpublished study (modeling) for Lyondell Chemical Co., 24 October 2003.

(3) Bridie, AL, Wolff, CJM and Winter, M (1979) BOD and COD of some petrochemicals. Water Research 13, 627-630.

(4) Bridie, AL, Wolff, CJM and Winter, M (1979) The acute toxicity of some petrochemicals to goldfish. Water Research 13, 623-626.

(5) Callander, R.D. (2004). Allyl alcohol: Bacterial mutagenicity assay in S. typhimurium and E. coli. CTL Study Number YV6638. Central Toxicology Laboratory, Cheshire, UK. Sponsored by Hercules Incorported, Wilmington, DE.

(6) Carpanini, FMB, Gaunt, IF, Hardy, J, Gangolli, SD, Butterworth, KR and Lloyd, AG (1978) Short-term toxicity of allyl alcohol in rats. Toxicol. 9, 29-45.

(7) Carpenter, CP and Smyth, HF (1946) Chemical burns to the rabbit cornea. Am J Opthalmology 29, 1363-1372.

(8) Carpenter, CP, Smyth, HF, and Pozzani, UC (1949) The assay of acute vapor toxicity, and the grading and interpretation of results on 96 chemical compounds. J Ind Hyg Toxicol 31, 343-346.

(9) Clay, P. (2004). Allyl alcohol: L5178Y TK+/- mouse lymphoma mutation assay. CTL Study Number VV0306. Central Toxicology Laboratory, Cheshire, UK. Sponsored by Hercules Incorporated, Wilmington, DE.

(10) Dunlap, MK, Kodama, JK, Wellington, JS, Anderson, HH and Hine, CH (1958) The toxicity of allyl alcohol. AMA Archives of Industrial Health 18, 303-311.

(11) EPI Suite (^TM) v.3.10 (2000) US-EPA Office of Pollution Prevention and Toxics and Syracuse Research Corporation.

(12) Ewell, WS, Gorsuch, JW, Kringle, RO, Robillard, KA and Spiegel, RC (1986) Simultaneous evaluation of the acute effects of chemcials on seven aquatic species. Envir Tox Chem 5, 831-840.

(13) Fox, V. (2004). Allyl alcohol: In vitro cytogenetics assay in human lymphocytes. CTL Study Number SV1223. Central Toxicology Laboratory, Cheshire, UK. Sponsored by Hercules Incorporated, Wilmington, DE.

(14) Grosjean, D, Grosjean, E and Williams, EL (1993) Atmospheric chemistry of unsaturated alcohols. Environ Sci Technol 27, 2478-2485.

(15) Grosjean, D, Grosjean, E and Williams, EL (1993) Rate constants for the gas-phase reactions of ozone with unsaturated alcohols, esters, and carbonyls. Int J Chem Kinetics 25, 783-794.

(16) Hicks, S.L. (2005). Acute toxicity of allyl alcohol 20906MB (Lyondell lot number CX30609214) to the water flea, Daphnia magna, determined under static-renewal test conditions. ABC Study No. 48909, ABC Laboratories, Inc., Columbia, Missouri. Sponsored by the Lyondell Chemical Company, Houston, TX.

(17) Hicks, S.L. (2005). Toxicity of allyl alcohol 20906MB (Lyondell lot number CX30609214) to the unicellular green alga, Psudokirchneriella subcapitata. ABC Study No. 48910, ABC Laboratories, Inc., Columbia, Missouri. Sponsored by the Lyondell Chemical Company, Houston, TX.

(18) Howard, PH (1989) Allyl Alcohol. In Handbook of Environmental Fate and Exposure Data for Organic Chemicals. Lewis Publishers, pp38-43

(19) Howard, PH, Boethling, RS, Jarvis, WF, Meylan, WM and Michalenko, EM (1991) Handbook of environmental degradation rates.

(20) Huekelekian, H and Rand, MC (1955) Biochemical oxygen demand of pure organic compounds. Sewage and Industrial Wastes 27, 1040-1053.

(21) Hustert, K and Parlar, H (1981) Ein testverfahren zum photochemischen abbau von umweltchchemikalien in der gasphase. Chemosphere 10, 1045-1050.

(22) Jacobs, GA and Martens, MA (1989) An objective method for the evaluation of eye irritation in vivo. Fd Chem Toxic 27, 255-258.

(23) Jenkinson, PC and Anderson, D (1990) Malformed foetuses and karyotype abnormalities in the offspring of cyclophosphamide and allyl alcohol-treated male rats. Mut Res 229, 173-184.

(24) Jenner, PM, Hagan, EC, Taylor, JM, Cook, EL and Fitzhugh, OG (1964) Food flavourings and compounds of related structure. I. Acute oral toxicity. Fd Cosmet Toxicol 2, 327-343.

(25) JETOC (1992) Biodegradation and bioaccumulation data of existing chemicals based on the CSCL Japan. Japan Chemical Industry Ecology-Toxicology and Information Center (JETOC), complied under the supervision of the Chemical Products and Safety Division, Basic Industries Bureau, Ministry of International Trade, Japan.

(26) Lijinsky, W and Andrews, AW (1980) Mutagenicity of vinyl compounds in Salmonella typhimurium Terat Carc Mutagen 1, 259-267.

(27) Lijinsky, W and Reuber, MD (1987) Chronic carcinogenesis studies of acrolein and related compounds. Toxicol Ind Hlth 3, 337-345.

(28) Lipnick, RL, Watson, KR and Strausz, AK (1987) A QSAR study of the acute toxicity of some industrial organic chemicals to goldfish. Narcosis, electrophile and proelectrophile mechanisms. Xenobiotica 17, 1011-1025.

(29) Lutz, D, Eder, E, Neudecker, T and Henschler, D. (1982) Structure-activity relationships in a,B-unsaturated carbonylic compounds and thier corresponding allylic alcohols. Mut res 93, 305-315.

(30) Lyondell Chemical Company (2003) Allyl Alcohol - Product Safety Bulletin, November 2003, pp69.

(31) Lyondell Chemical Company (undated) Product Application Data for Alyl Alcohol, pp2.

(32) McCord, CP (1932) The toxicity of allyl alcohol J Am Med Assoc 98, 2269-2270.

(33) Meylan, WM, Howard, PH, Boethling, RS, Aronson, D, Printup, H and Gouchie, S (1999) Improved method for estimating bioconcentration/bioaccumulation factor from octanol/water partition coefficient. Environ Toxicol Chem 18, 664-672.

(34) NTP unpublished results (ntp-server.niehs.nih.gov/)

(35) Patel, JM, Gordon, WP, Nelson, SD and Leibman, KC (1983) Comparison of hepatic biotransformation and toxicity of allyl alcohol and [1,1-2H2]allyl alcohol in rats. Drug Metab Disp 11, 164-166.

(36) Principe, P, Dogliotti, E, Bignami, M, Crebelli, R, Falcone, E, Fabrizi, M, Conti, G and Comba, P (1981) Mutagencicity of chemcials of industrial and agricultural relevance in Salmonella, Streptomyces and Aspergillus. J Sci Fd Agric 32, 826-832.

(37) Reid, W (1972) Mechanism of allyl alcohol-induced hepatic necrosis. Experientia 28, 1058-1061.

(38) Sangster, J (1989) Octanol-water partition coefficients of simple organic compounds. J Phys Chem Ref data 18, 1111-1229.

(39) Slott, VL and Hales, BF (1985) Teratogenicity and embryolethality of acrolein and structurally related compounds in rats. Teratology 32, 65-72.

(40) Smith, AM, Mao, J, Doane, RA and Kovacs, MF (1995) Metabolic fate of [14]CAcrolein under aerobic and anaerobic aquatic conditions. J Agric Fd Chem 43, 2497-2503.

(41) Smith, RA, Cohen,SM and Lawson, TA (1990) Acrolein mutagenicity in the V79 assay - short communication. Carcinogenesis 11, 497-498.

(42) Smyth, HF and Carpenter, CP (1948) Further experience with the range finding test in the industrial toxicology laboratory. J Ind Hyg Toxicol 30, 63-68.

(43) Stump, D.G. (2005). A prenatal developmental toxicity study of allyl alcohol in rats. Study Number - WIL-14038, WIL Research Laboratories, LLC., Ashland, OH. Sponsored by the Lyondell Chemical Company, Houston, TX.

(44) Verschueren, K (1996) Handbook of Environmental Data on Organic Chemicals, Van Nostrand Reinhold NY, p158.

(45) Weast, RC and Astle, MJ (1985) CRC Handbook of Data on Organic Compounds, Vol.1, CRC Press, Inc Boca Raton, Fl, p603.

(46) Windholz, M, Budavari, S, Blumetti, RF and Otterbein, ES (1983) The Merck Index, 10th Edition,Merck and Co., Inc, Rahway NJ, p277.

10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT